"STUDIES IN THE FLUORENE SERIES"

By

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PREFACE

This thesis resulted from two years research training under the stimulating supervision of Dr. Neil Campbell. The writer is grateful to the Carnegie Trust for the Universities of Scotland for a scholarship which made this work possible and to his friends, especially A. Marks and T.R.R. Macdonald, who endured many monologues on the subject of fluorene chemistry. Thanks are also due to Dr. James Blair who first sublimed indone oxime while studying high vacuum techniques, and to Norman Keir, B.Sc., who assisted with many experiments on the enolbetaines. Throughout the period of active research and of subsequent thesis writing, Dr. Campbell has contributed liberally not only with many excellent suggestions but with encouragement and advice; acknowledgement is made of this and his kindness and good humour which made the research a pleasant experience.

Cambridge,

May 1951.

STUDIES IN THE FLUORENE SERIES

INTRODUCTION

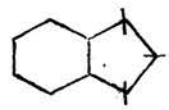
Studies in the chemistry of fluorene and related hydrocarbons are important not because of any industrial or medical potentialities but because of the manner in which they alter the perspective in which the fundamental problems of aromatic chemistry are viewed. During the last century the changes in conceptions of valency have caused continual refocussing of attention and opinion on the chemist's interpretations of the theoretical bases of aromatic properties. The fertility of the modern theory of resonance and of the wave mechanical interpretations of mesomerism cannot be questioned but the general applicability of their conclusions must be proved. This can only be done by applying them to series of aromatic compounds containing not only six-membered benzenoid rings but other constitutional factors, for it was on a basis of the study of compounds containing only benzenoid rings that the origin of these theoretical approaches occurred. In this thesis the principal consti-

tutional factor to be examined is the five-membered ring in condensed polycyclic hydrocarbons of aromatic type. Fluorene has been selected for principal, although not exclusive, attention.

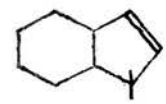
The Fluorene Series: The stricter interpretation of the term "fluorene series" meaning fluorene and its simpler derivatives is not employed; the fluorene series is defined in two ways.

(A) Fluorene is a member of a group of polycycles based on the cyclopentadiene structure, I. The principal hydrocarbons of this series are hydrindene, II(a), indene, II(b), fluorene, III, phenanthrindene, IV, acenaphthene, V(a), acenaphthylene, V(b), fluoranthene, VI and the two as yet unknown, but nevertheless important, hydrocarbons, VII and, VIII.

I



II(a).



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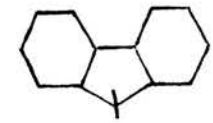

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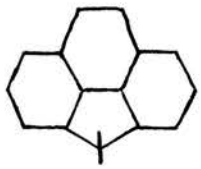

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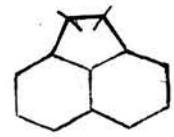
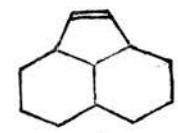


V(a)



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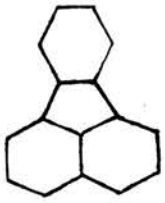

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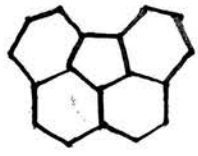
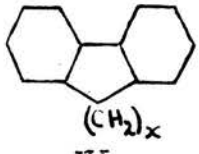


VII

VIII

(B) Fluorene is a member of the 2;2'-polymethylenebiphenyl series whose general formula is IX. When x = 0 the series member may be regarded as either biphenyl, X, or biphenylene, XI. When x = 1 the series member is fluorene, III; when x = 2 it is 9:10-dihydrophenanthrene, XII, and when x = 3 it is dibenzocycloheptadiene, XIII.



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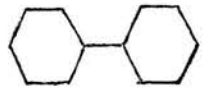
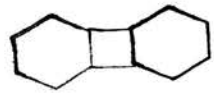
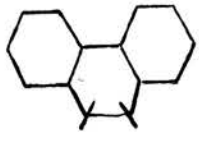


X



XI



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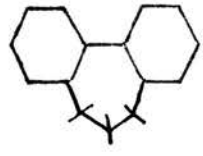


XIII

The Nature of the Studies: The studies fall into two parts. Part I is an attempt to coordinate many of the known facts regarding the chemistry and structure of fluorene with the many facts known about related compounds. The structural homology is discussed as fully as possible and an attempt is made to clarify many of the inherent problems in this field. Although some aspects of the discussion of the chemistry of certain of the hydrocarbons listed above may be regarded as irrelevant, they are included to provide continuity to the background from which conclusions are derived.

Part II involves new experimental work in the fluorene series. Much of the trouble in the study of fluorene chemistry arises from the difficulty of synthesising the required derivatives. Sections I and III describe investigations of certain routes to the synthesis of fluorene compounds. Section II is an investigation of the substitution reactions of 2-aminofluorene. In section I studies of certain hydrindene derivatives of the enolbetaine type are discussed. The latter studies are to some degree irrelevant but a new compound of aromatic type based on the hydrindene structure has been synthesised.

Many of the conclusions derived in Part II are discussed in Part I when they are relevant and materially aid any conclusion. The discussions in Part II are concerned with the more particular problems which arose during the experimental

work and with the indication of the chemical significance of the work apart from the fluorene series.

Literature: The chemistry of fluorene has been competently and exhaustively reviewed by Rieveschl and Ray (Chem.Rev., 1938, 23, 287 et.seq.). The chemistry of the remaining hydrocarbons, with the exception of biphenylene (Baker, Tilden Lecture, J., 1945, pp. 266), have not been reviewed in recent years, if at all. It has therefore been found necessary to indicate the salient features of their chemistry. The papers referred to are regarded as giving the significant chemical facts most effectively and are not necessarily selected because of chronological precedence.

PART I

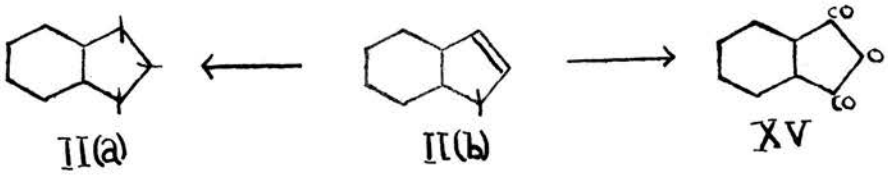
SECTION I

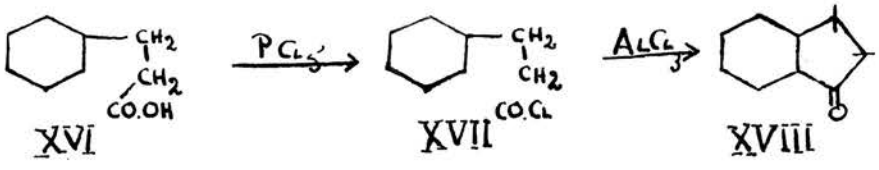
THE STRUCTURE OF FLUORENE AND RELATED HYDROCARBONS

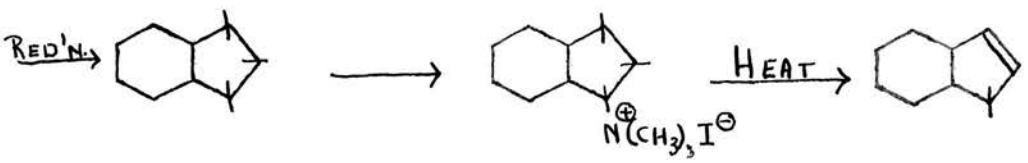
The structural elucidation of fluorene, III, is closely interwoven with that of phenanthrene, XIV, (Ray and Rieveschl, ibid, 288-294). The thoroughness with which Ray and Rieveschl describe the classical methods which culminated in the confirmation of the fluorene structure obviates any need to describe the work. The structure of the remaining hydrocarbons (with the exceptions of VII and VIII which are unknown) were determined in some cases by oxidative degradations and in the remainder by their syntheses. The most important methods used are briefly given in each case.

Hydrindene and indene:

SCHEME 1





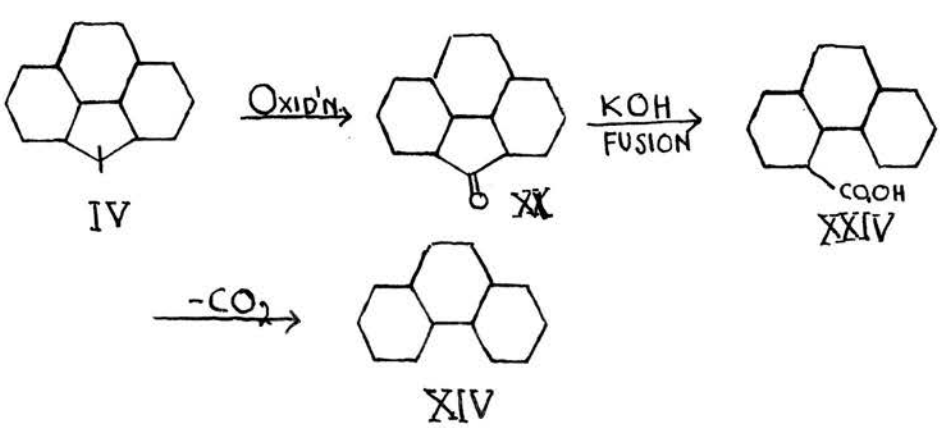


II(a) XIX II(b).

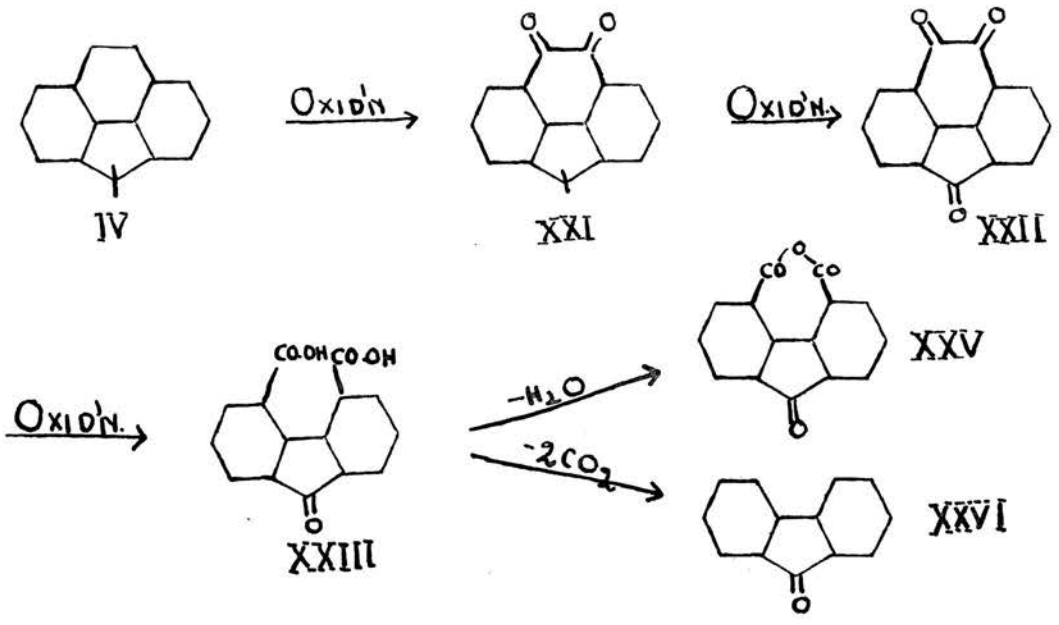
Indene, II(b), is reduced to hydrindene, II(a), by sodium in boiling alcohol (Kraemer and Spilker, Ber., 1890, 23, 3280). Oxidation of indene by 30% nitric acid gives phthalic acid, XV, which was isolated as the anhydride (Kraemer and Spilker, loc.cit.). 1-Hydrindone, XVIII, has been synthesised by Kipping (J., 1894, 480) from β-phenylpropionic acid, XVI, via the acid chloride, XVII. Packendorff, Leder-Packendorff and Zelinskii (Ber., 1934, 67B, 300-2) hydrogenated 1-hydrindone and obtained hydrindene in good yield. Kipping and Hall (J., 1900, 468) converted hydrindene via hydrindene-1-trimethylammonium iodide, XIX, to indene thus completing the syntheses, Scheme 1.

Phenanthrindene:

SCHEME 2



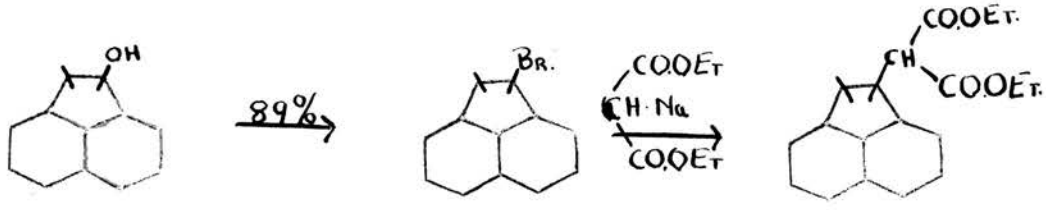
IV XX XXIV XIV

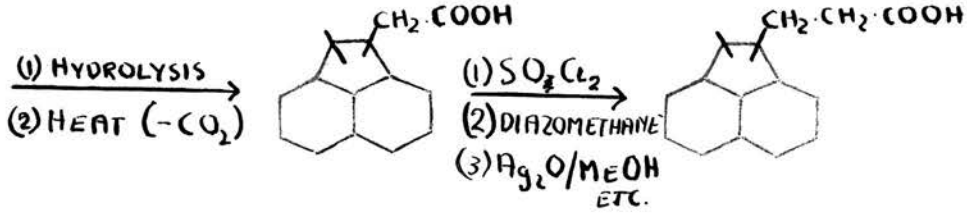


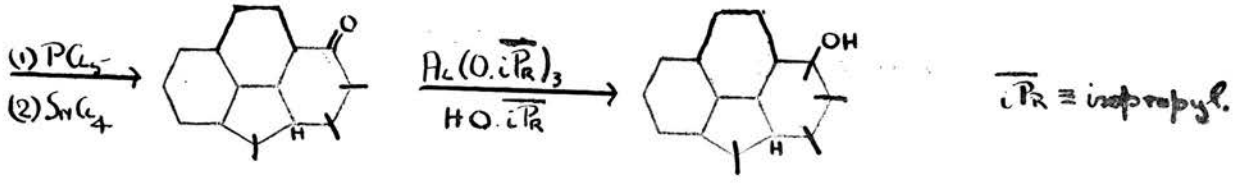
This hydrocarbon was isolated by O. Kruber from coal-tar (Ber., 1934, 67, 1000) and he identified it by Scheme 2 above. Its degradation was based on oxidative reactions, which, depending on the severity of the conditions, gave greater or lesser quantities of 4-ketophenanthrrindene, XX, 4: 5-methylenophenanthraquinone, XXI, 4:5-ketophenanthraquinone, XXII, fluorenone-4: 5-dicarboxylic acid, XXIII. XX on fusion with caustic potash gave phenanthrene-4-carboxylic acid which was decarboxylated to give phenanthrene, XIV. The fluorenone-4: 5-dicarboxylic acid gives an anhydride, XXV, and may be decarboxylated to give fluorenone, XXVI.

The synthesis of phenanthrindene, Scheme 3, in very good yield by Bachmann (W.E.) and Sheehan (J.A.C.S., 1941, 63, 204) is notable for its elegance and should assist further study of the hydrocarbon.

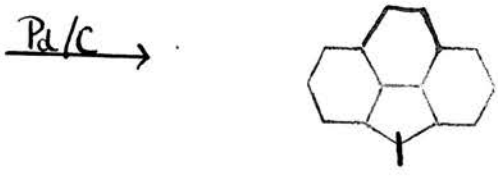
SCHEME 3







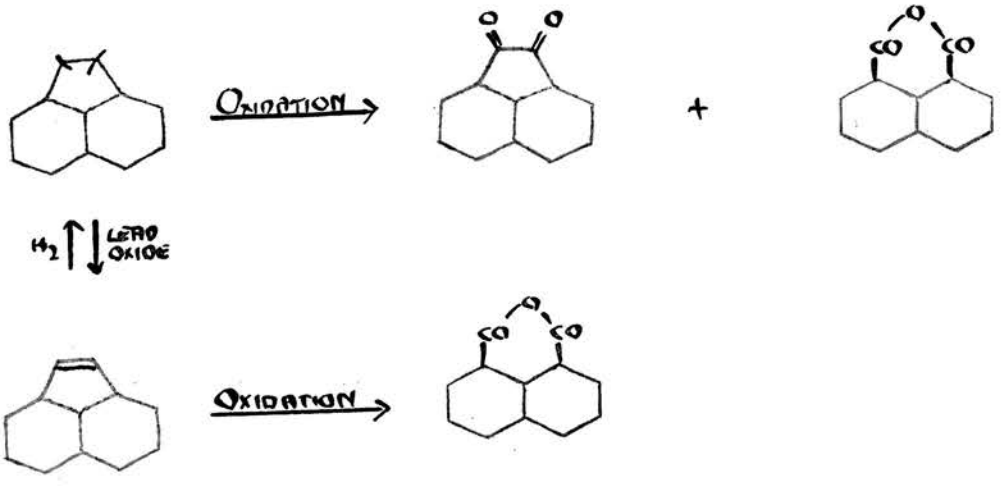
$\overline{iPr}$ ≡ isopropyl.



$+H_2O \quad + H_2.$

Acenaphthene and Acenaphthylene:

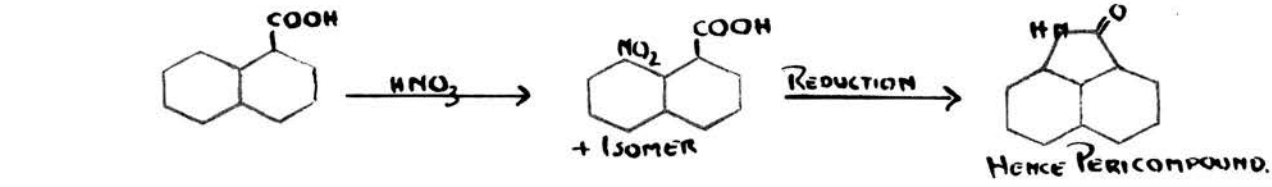
SCHEME 4

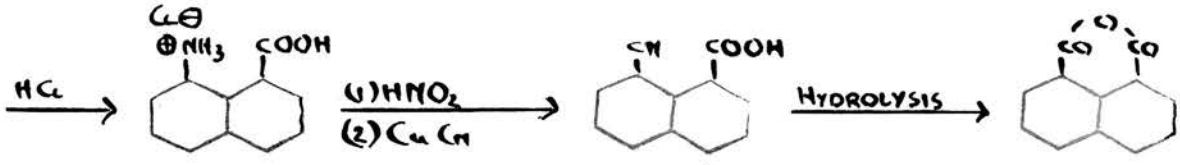


The oxidation of acenaphthene gives acenaphthenequinone and naphthalic anhydride (Graebe and Veillon, Ber., 1887, 20, 659). It has been converted to acenaphthylene by passage over heated lead oxide. The reversion has also been achieved by reduction with sodium amalgam in alcohol. Oxidation of acenaphthylene gives napthalic anhydride (Behr and van Dorp, Ber., 1873, 6, 753).

The structure of naphthalic acid was shown by Bamberger and Philip (Ber., 1887, 20, 243) by Scheme 5.

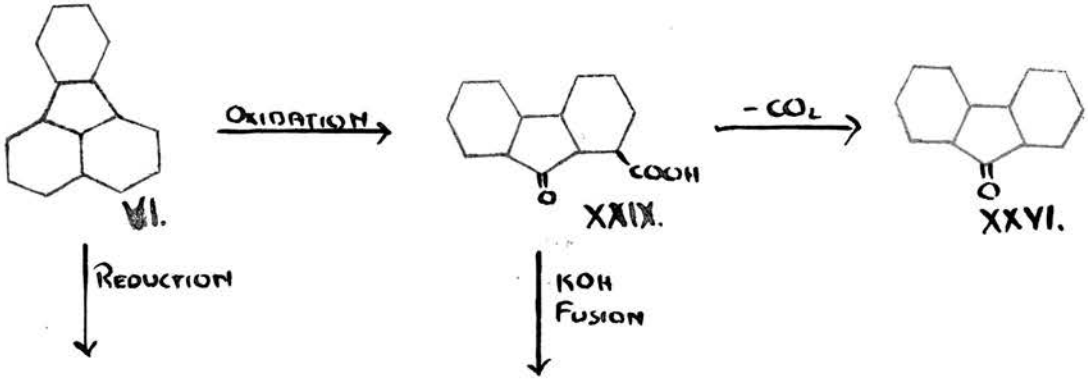
SCHEME 5

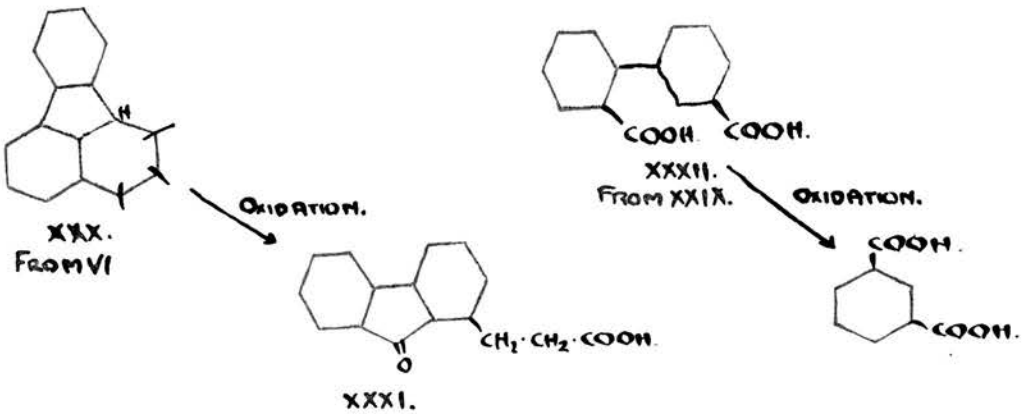




Fluoranthene: The relationship of fluoranthene to fluorene was demonstrated by Fittig and his co-workers (Fittig and Gebhard, Ber., 1877, 10, 2141; Ann., 1878, 193, 142; Fittig and Liepmann, Ber., 1879, 12, 163; Ann., 1880, 200, 1.). The essential evidence for the assigned structure is illustrated in Scheme 6.

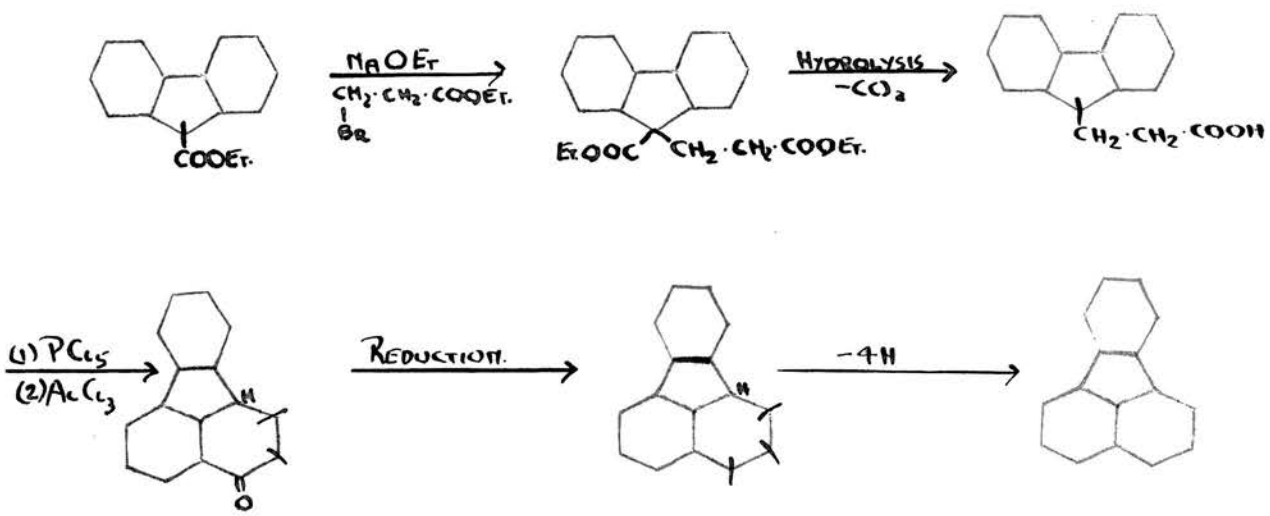
SCHEME 6





The synthesis of fluoranthene has been achieved in several ways. In Scheme 7 the method of von Braun and Anton (Ber., 1929, 62, 145) is illustrated.

SCHEME 7

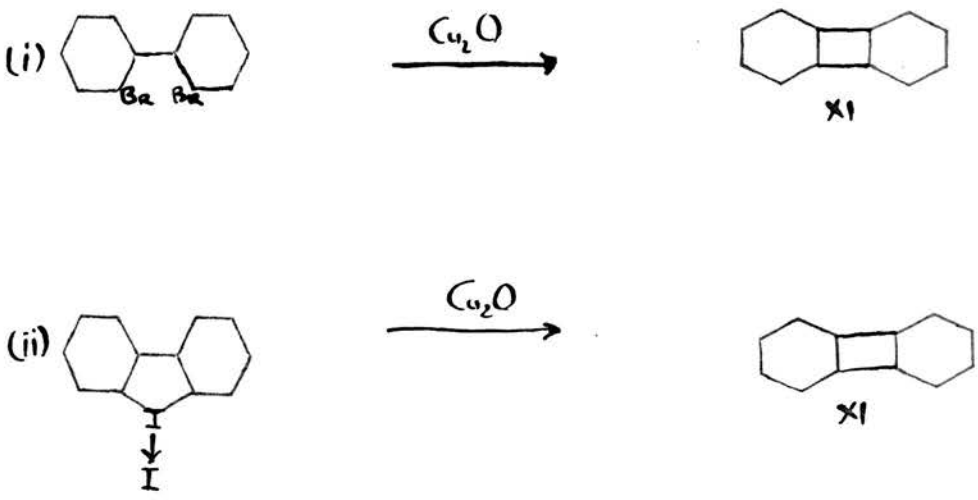


Biphenyl: The structure of biphenyl follows from its preparation from iodobenzene (Ullmann and Meyer, Ann., 332, 40), Scheme 8.

SCHEME 8

Biphenylene: The first convincingly successful preparation of this hydrocarbon was by Lothrop (J.A.C.S., 1941, 63, 1187) - Scheme 9.

SCHEME 9



In preparation (ii) biphenyleneiodonium iodide, XXXIV, was pyrolysed with cuprous oxide. The product analysed correctly for the biphenylene monomer. That no deep seated change had occurred was convincingly shown by Baker (loc.cit.) who reduced the hydrocarbon catalytically under mild conditions to biphenyl.

9:10-dihydrophenanthrene: This is produced by the catalytic reduction of phenanthrene over a copper chromite catalyst. (Mosettig and Burger, J.A.C.S., 1935, 57, 2731.)

Dibenzocycloheptadiene: This has been synthesised by Rapport and Williams (J.A.C.S., 1949, 71, 1774) who used several routes of which Scheme 10 is the most elegant.

SCHEME 10

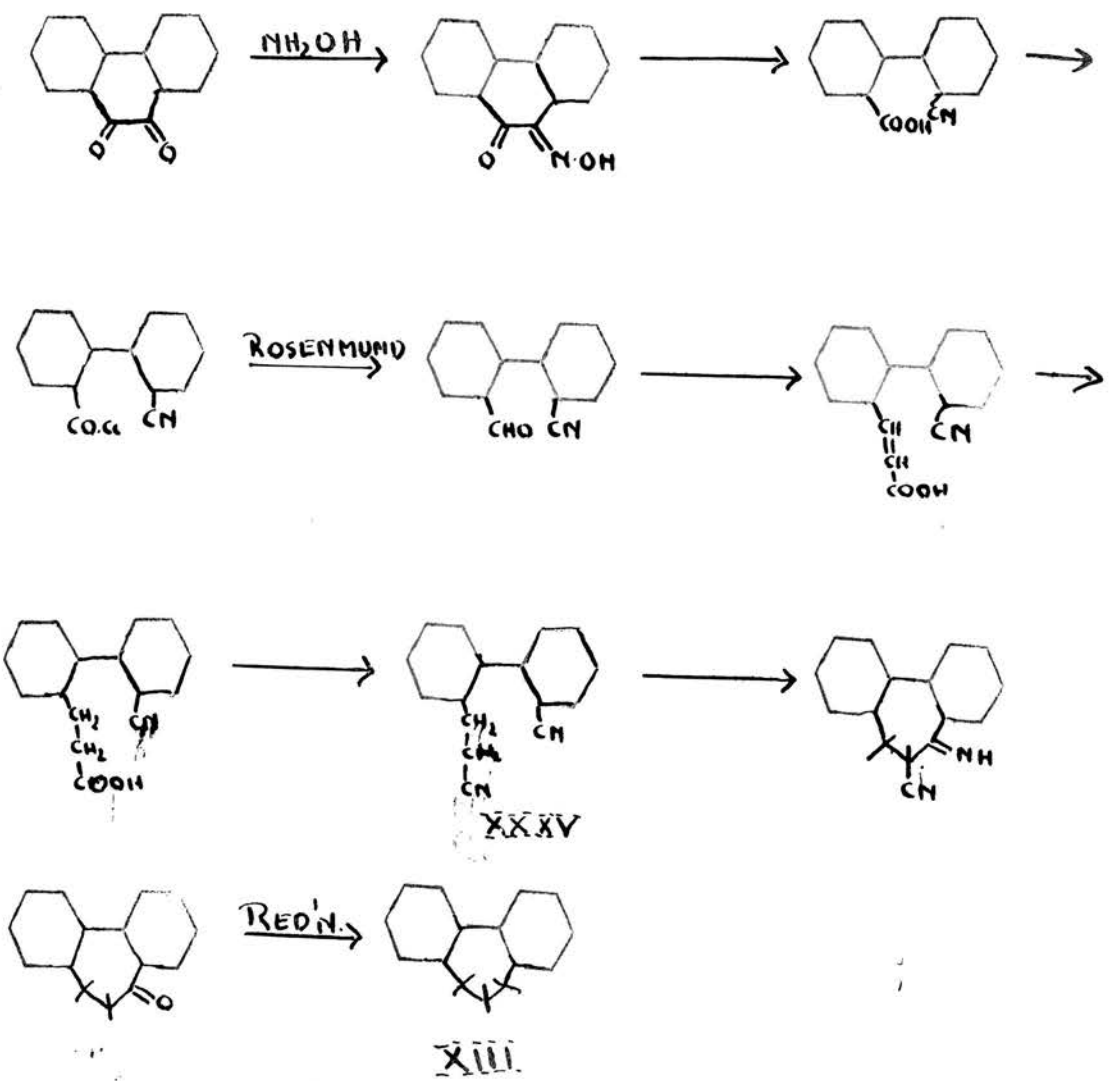


FIG I.

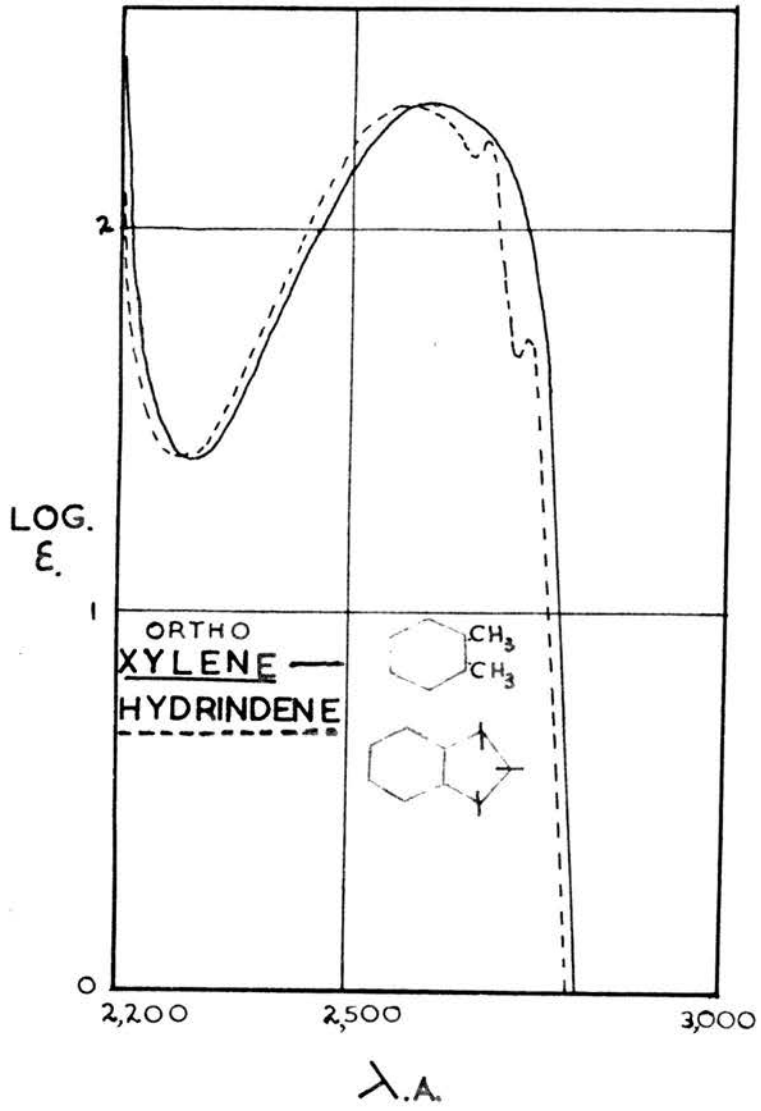
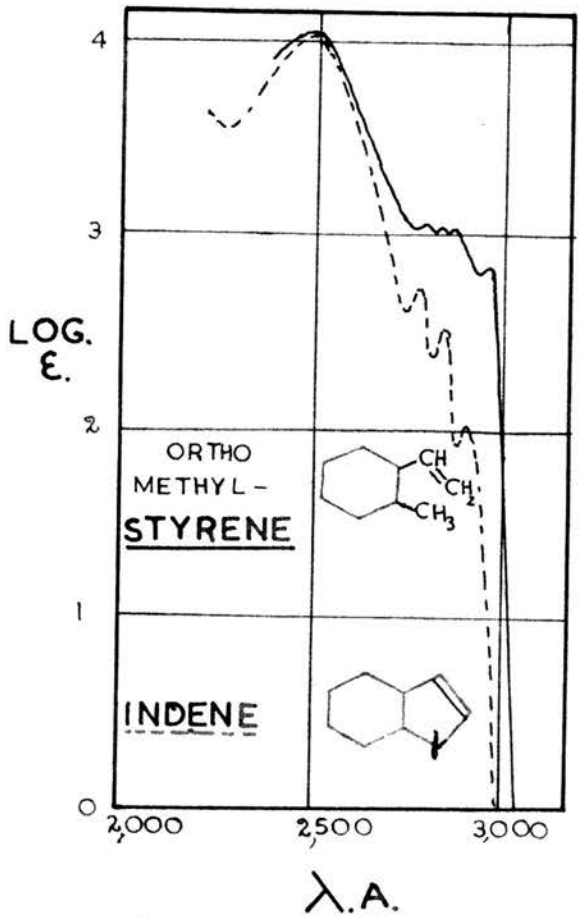

LOG. ε.
2
1
0
ORTHO
XYLENE
HYDRINDENE
CH3
CH3
2,200
2,500
3,000
λ.A.

FIG II


LOG. ε.
4
3
2
1
0
ORTHO
METHYL-
STYRENE
INDENE
CH
CH2
CH3
2,000
2,500
3,000
λ.A.

The cyclisation of 2-cyano-2'-biphenyl-β-propionitrile, XXXV, was by the method of Ziegler, Eberle and Ohlinger (Ann., 1933, 504, 94).

Comparative aspects in the study of the hydrocarbons of the fluorene series

Selected members of the series are compared with similar compounds which do not possess a five-membered ring, e.g. o-Xylene and hydrindene, styrene and indene. The conclusions reached are coordinated and an attempt is made to assess the influence of the five-membered ring. In this section physical characteristics only are considered.

o-Xylene and hydrindene: The absorption spectra of these two compounds have been contrasted by Ramart-Lucas and Hoch (Bull. Soc., 1935, 2, [5], 330). The absorption curves, Fig. I, are similar, differing only in so far as hydrindene has several fine bands.

The resonance energies of hydrindene and benzene have been contrasted by Brockway and Taylor (Ann.Reps., 1937, 215). The work is dependent on the calorific determination of the heat evolved in hydrogenating the hydrocarbons, Table I.

TABLE I

The heat evolved ($-\Delta H$) is tabulated for the listed compounds; x represents the number of molecular proportions of hydrogen absorbed

x	Compound	$(-\Delta H)$
x = 1	cyclohexene	28.59 Kil.cals/mole.
x = 3	benzene	49.80
	ethylbenzene	48.92
	o-xylene	47.25
	mesitylene	47.62
	hydrindene	45.80
x = 4	styrene	77.48
	indene	69.91

The resonance energy E is calculated as follows:

$$E = -\Delta H_{\text{compound}} - 3\left[(-\Delta H)_{\text{cyclohexene}}\right] - F_{\text{subst.}}$$

where $F_{\text{subst.}}$ is a factor which takes the effect of the substituents on the heat of hydrogenation.

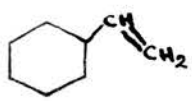
$E_{\text{benzene}} = 49.80 - 3 \times 28.59 - 0 = -36.0$ Kil.cals/mole.

$E_{\text{hydrindene}} = 45.80 - 3 \times 28.59 - 2.6 = -37.4$ Kil.cals/mole.

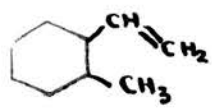
Brockway and Taylor do not consider that the difference is significant but in any case the higher value for hydrindene would indicate a higher degree of resonance stabilisation.

Indene, styrene (XXXVI) and o-methylstyrene (XXXVII):

II(b).



XXXVI.



XXXVII.

The absorption spectra of indene and o-methylstyrene have been compared by Ramart-Lucas and Hoch (loc.cit.). The curves, Fig. II, indicate that ring closure of XXXVII to give II(b) does not cause a very great change in the absorption. The relative degree of interaction of the double bonds and the benzene ring is more significantly indicated by comparison of the heats of hydrogenation of styrene and indene. In Table I it is noticeable that:

$$(-\Delta H)_{\text{styrene}} - (-\Delta H)_{\text{ethylbenzene}} = 29.56 \text{ Kil.cals/mole.}$$

whereas $(-\Delta H)_{\text{indene}} - (-\Delta H)_{\text{hydrindene}} = 24.11$ Kil.cals/mole.

i.e. the heat evolved in hydrogenating styrene to ethyl benzene is greater than that evolved in hydrogenating indene to hydrindene. These figures are not quite comparable, however, since the difference viz 5.45 Kil.cals/mole. should be compared with the difference between the heats of hydrogenation of cyclopentene and n-butene (30.3 - 26.9) Kil.cals/mole. which is 3.4 Kil.cals/mole. This on comparison with the value 5.45 would indicate that indene is more aromatic than styrene but the energy difference (2.1 Kil.cals. per mole.) is not of a high order.

FIG. III(a).

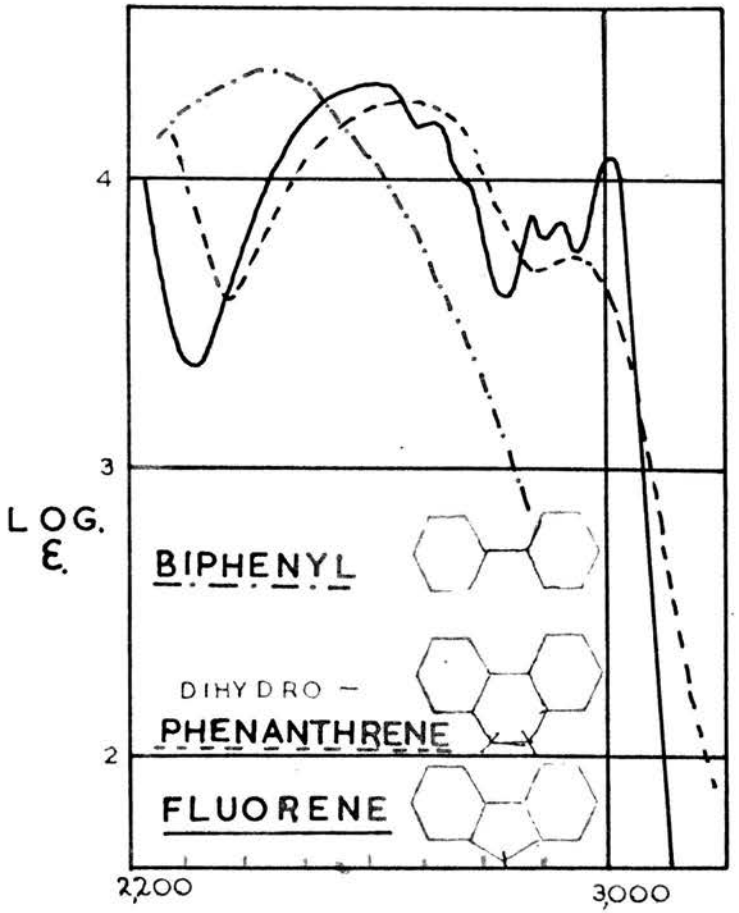
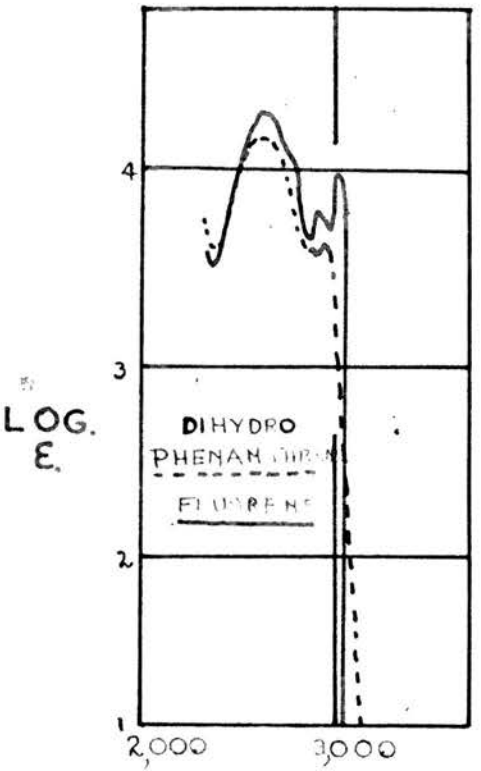


FIG III(b).



Fluorene, biphenyl and 9; 10-dihydrophenanthrene:

The absorption spectra of these three compounds have been compared by R.N. Jones (J.A.C.S., 1945, 67, 2130), Fig. III(a). The principal differences are:

(1) that biphenyl absorbs most strongly at shorter wavelengths than the others,

and (2) that the curve for fluorene, although it is similar to that of dihydrophenanthrene has more fine structure.

The curves given by Jones should be compared with those of Askew (J., 1935, 513) in which the maxima at 2900Å and $\log_{10}\varepsilon_{max.}$ = c.3.9 for dihydrophenanthrene is resolved into two small maxima, Fig. III(b).

The polarography of fluorene, dihydrophenanthrene and biphenyl has been studied by Wawzonek and Laitinen (J.A.C.S., 1942, 64, 2365-8).

> "Aromatic compounds possessing a high degree of resonance such as benzene, do not undergo reduction at the dropping mercury electrode. On the other hand, aromatic polynuclear hydrocarbons showing a diminished degree of resonance are reducible."

Selected examples are chosen from their work and contrasted in Table II. $\Pi_{\frac{1}{2}}$ represents the half wave potential for the reductions and I_D represents the diffusion current constants measured under similar conditions. Of these the

most significant for the present discussion is $\Pi_{\frac{1}{2}}$ volts. Wawzonek and Laitinen picture the reduction of fluorene, dihydrophenanthrene and biphenyl as being a 1:4 addition to the biphenyl system of each molecule represented generally below.

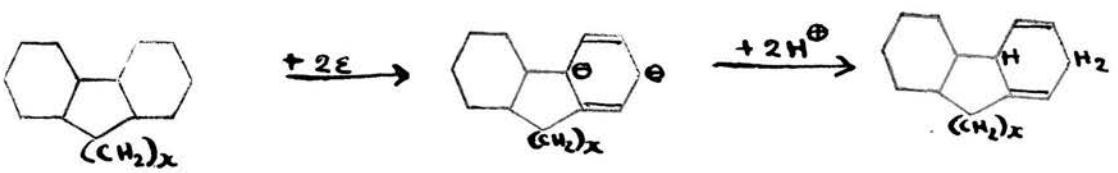
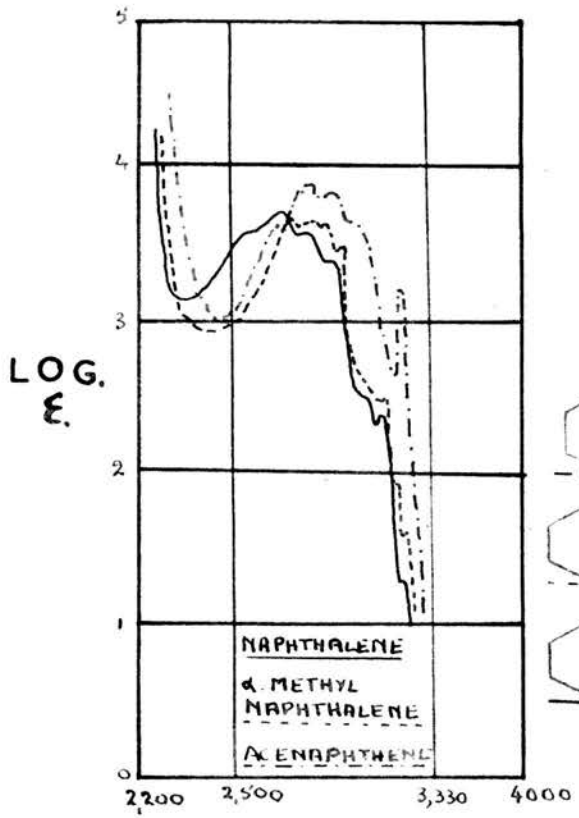


TABLE II

Compound	$\Pi_{\frac{1}{2}}$ volts	I_D
Anthracene	1.94	4.47
Acenaphthene	2.57	4.91
Naphthalene	2.50	5.15
Fluorene	2.65	5.65
Biphenyl	2.70	6.96
9; 10-dihydrophenanthrene	2.62	7.18

Although the comparison of the results of Table II must be done carefully, it is apparent that $\Pi_{\frac{1}{2}}$ must be characteristic of the ease of reduction and give an indication of the relative ease of reduction of related compounds. It is apparent that the ease of reduction of

FIG. IV(b).



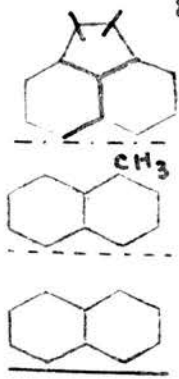
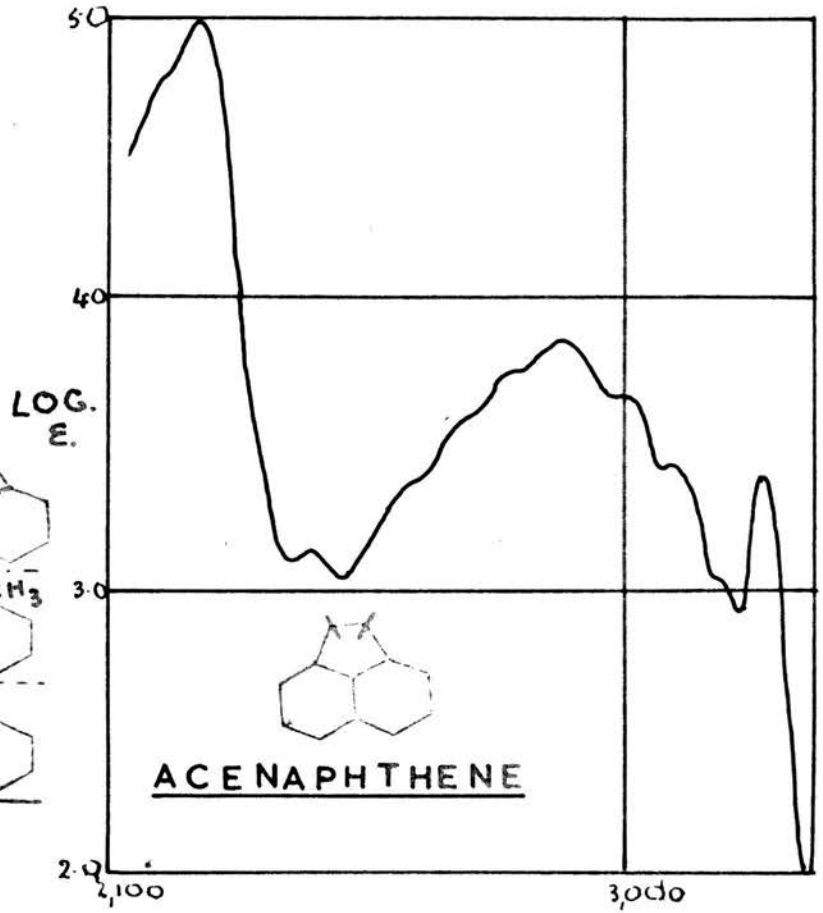


FIG. IV(a).

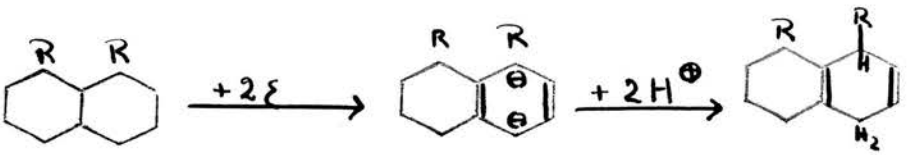


fluorene is intermediate between that of 9:10-dihydrophenanthrene and biphenyl, the one that is least readily reduced. The low value of Γ_o for fluorene will be discussed (page) when the dipole studies of fluorene are discussed.

Acenaphthene and naphthalene:

The absorption spectra of acenaphthene, α-methylnaphthalene and naphthalene have been contrasted by Pestemer and Manchen (Monatsh., 1936, 68, 94), Fig. IV. There is an obvious similarity in the curves, all of which are rich in fine banding. Acenaphthene absorbs at a longer wavelength than the other two but there is a close similarity in form. Certain of the smaller maxima are more accented in the case of acenaphthene.

The results of polarographic studies on acenaphthene and naphthalene are shown in Table II. In this case the reduction process is a 1:4 reduction of the naphthalene nucleus



The results for acenaphthene (R = $>CH_2$) and naphthalene (R = H) are not completely comparable as the lack of experience cannot permit the discussion of the influence of the methylene substituent attached to the site of substitution in acenaphthene.

Conclusions:

(1) Examination of the absorption spectra of fluorene and dihydrophenanthrene, and, of hydrindene and o-xylene, indicate that the introduction of a five-membered ring causes the development of fine structure (i.e. several slender maxima) in the absorption curves. In the case of naphthalene and acenaphthene this is apparently only manifested by the accentuation of several slender maxima already present in the naphthalene curves.

(2) Examination of the absorption spectra of fluorene, biphenyl and dihydrophenanthrene shows that the shift of absorption to longer wavelengths in the case of fluorene and dihydrophenanthrene is due principally to the effective substitution of biphenyl in the 2,2' positions. In the case of fluorene the bathochromic shift relative to biphenyl cannot be explained to any large extent by the interaction of the two benzenoid rings through the 9-methylene group, for in the case of dihydrophenanthrene where such interaction would be negligible the absorption curve is similar to that of fluorene.

o-Xylene and hydrindene absorb at very closely the same wavelengths, hence the 5-membered ring has only a minor effect on the energy of the excitation change occurring on absorption, although from (1) it causes the partial resolution of the general absorption curve into discrete maxima.

(3) Heats of hydrogenation and the derived resonance energies indicate that there is little difference between the resonance stabilisation of hydrindene, o-xylene and benzene. Similar studies on indene and styrene indicate that there is greater interaction between the alicyclic double bond and the benzene ring (indene) than between the extracyclic double bond and the benzene ring (styrene). This causes the resonance energy of indene to be greater than that of styrene and increases the relative stability of indene.

(4) Acenaphthene absorbs at longer wavelengths than naphthalene and its simpler derivatives, although the general form of the curve is the same. This difference must be significant and indicates that, relative to naphthalene, the excitation energies for corresponding electronic changes are lower, although, because $\log \varepsilon$ possesses the same order of magnitude, the probability of the excitation is in both cases similar.

(5) Polarographic studies indicate that the energy of the changes occurring on reduction of fluorene, biphenyl and dihydrophenanthrene at the dropping mercury electrode are of similar magnitude, indicating that the reduction process is the same for these hydrocarbons. Fluorene holds a position between dihydrophenanthrene and biphenyl when the relative ease of reduction is considered.

(6) Polarographic studies of acenaphthene and naphthalene are insufficient to permit any detailed conclusions as the results for the reduction of peridialkylnaphthalenes are not available.

The physical evidence indicates that the presence of a five-membered ring in condensed polycyclic hydrocarbons makes very little difference to the properties of the molecule. The presence of small maxima in the absorption curves of compounds containing a five-membered ring is the only apparent difference from the properties of related compounds which do not possess a five-membered ring. The differences in the reduction characteristics can be explained by considering the effective differences in the substituents of the compared compounds rather than by considering the absence or presence of such a structural feature as a five-membered ring.

SECTION II

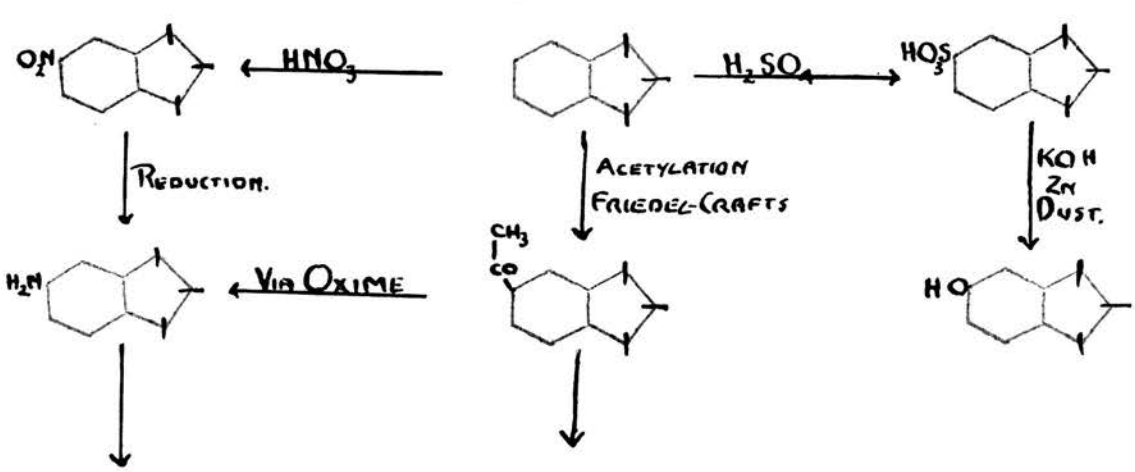
THE SUBSTITUTION REACTIONS OF FLUORENE AND RELATED HYDROCARBONS

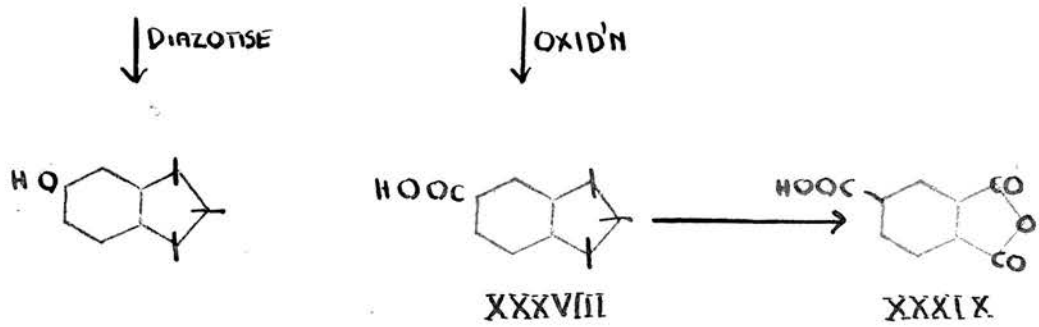
In this section typical substitution reactions of the various hydrocarbons will be described and the influence of different primary substituents on polysubstitution will be considered. Any evidence of "abnormal" substitution, i.e. reaction in an unusual position, will be indicated and discussed. Except in the case of fluorene, when details will be given, the evidence on which the orientation of the substitution products is assigned, will only be outlined and references given. No exhaustive survey is made - the substitution reactions of fluorene and its derivatives are fully discussed by Rieveschl and Ray (Chem. Revs., 1938, 23, 302, et seq.); the examples cited are either typical or of interest because of their exceptional nature. Some of the work discussed is to be found in Part II of this thesis to which cross-references are made.

Hydrindene

Hydrindene suffers sulphonation (Spilker, Ber., 1893, 26,1538) chiefly in the 5 position (80% 5 sulphonic acid, Cook and Linstead J., 1934, 946) but a small fraction of the 4-isomer is produced. Similarly, nitration occurs principally in the 5 position but also to some extent in the 4 position (v. Braun, Arkuszewski and Kohler, Ber., 1918, 51,282). The Friedel-Crafts acetylation occurs principally in the 5 position (Borsche and Pommer, Ber., 1921, 54,108) and this acetyl derivative, orientated by oxidation to hydrindene-5-carboxylic acid, XXXVIII, and further to trimellitic acid, XXXIX, has been used (Borsche and John, Ber., 1924, 59,656) to prepare pure 5-aminohydrindene by the Beckmann transformation of the oxime. This amine is the key to the orientation of the 5-sulphonate and 5-nitro compound as illustrated in Scheme 11. By elimination, the other isomer isolated must be the 4 derivative.

SCHEME 11





XXXVIII XXXIX

Fluorene

The reactions of fluorene fall into two groups:

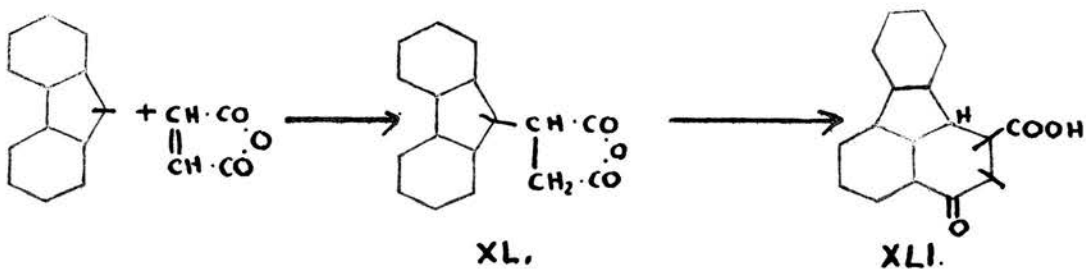
(A) the reactions of the methylene group,

and (B) the reactions of the "nucleus", i.e. the biphenyl framework of the molecule.

(A) The methylene group is characterised by the reactivity of the hydrogen atoms. Fluorene readily forms derivatives with alkali metals, e.g. the potassium derivatives (Weissgerber, Ber., 1901, 34, 1659). The activity is further demonstrated by the Zerewitinoff reaction (Zerewitinoff, Ber., 1912, 45, 2384) in which 1.04 moles. methane are released per mole. of fluorene. Like all compounds possessing a reactive methylene group fluorene undergoes certain condensation reactions usually in the presence of basic catalysts. The condensation of fluorene with aldehydes (Thiele, Ber., 1900, 33, 851), nitrosobenzene (Novelli., Abs., 1928, 22, 775) and diethyl oxalate (Wislicenus, Ber., 1900, 33, 771) are well known, but recently Bergmann and Orchin (J.A.C.S., 1949, 71, 1917) have

investigated the condensation of maleic anhydride and fluorene in the presence of basic catalysts. The product, XL, was cyclised to 3-keto-1a; 1; 2; 3-tetrahydrofluoranthene-1-carboxylic acid, XLI, Scheme 12.

SCHEME 12

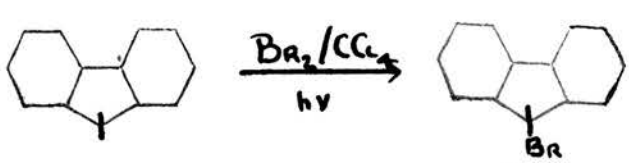


XL. XLI.

Halogenation of the 9-methylene group:

The hydrogen atoms may be replaced by halogen atoms

(i) By direct substitution: Sampey and Reid (J.A.C.S., 1947, 69, 234) have shown that 64% yields of pure 9-bromofluorene, XLII, may be obtained by direct bromination of fluorene in carbon tetrachloride under a mercury arc lamp.

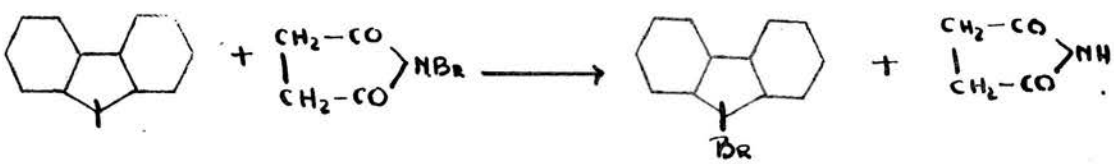


XLII.

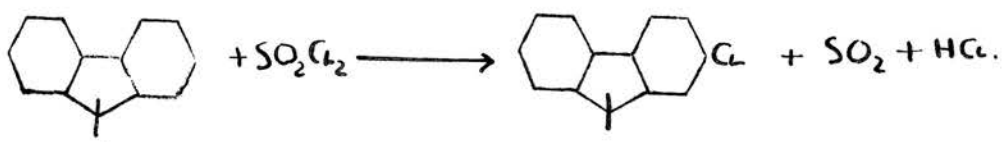
(ii) By reaction with N-bromosuccinimide. Wittig and Felletschin (Ann., 1944, 555, 133-4) claim that 9-bromofluorene is produced in yields up to 75% by reacting fluorene and

N-bromosuccinimide in carbon tetrachloride. It is significant that Kharasch and Brown (J.A.C.S., 1939, 61, 2145) have shown that sulphuryl chloride reacts with fluorene but nuclear substitution occurs. Sulphuryl chloride has been shown by these workers to be effective in substituting the side-chains of aromatic hydrocarbons (e.g. in m-Xylene or triphenyl methane). β-methyl naphthalene resembles fluorene in the greater reactivity of the nucleus.

SCHEME 13



However



(B) Nuclear Substitution

(α) Monosubstitution.

Nuclear monosubstitution occurs generally in the 2 position

(i) Chlorine, in the presence of iodine, reacts with

fluorene in benzene solution at 80°C to give 2 chlorofluorene in good yield (Buffle, H.C.A., 1932, 15, 1483).

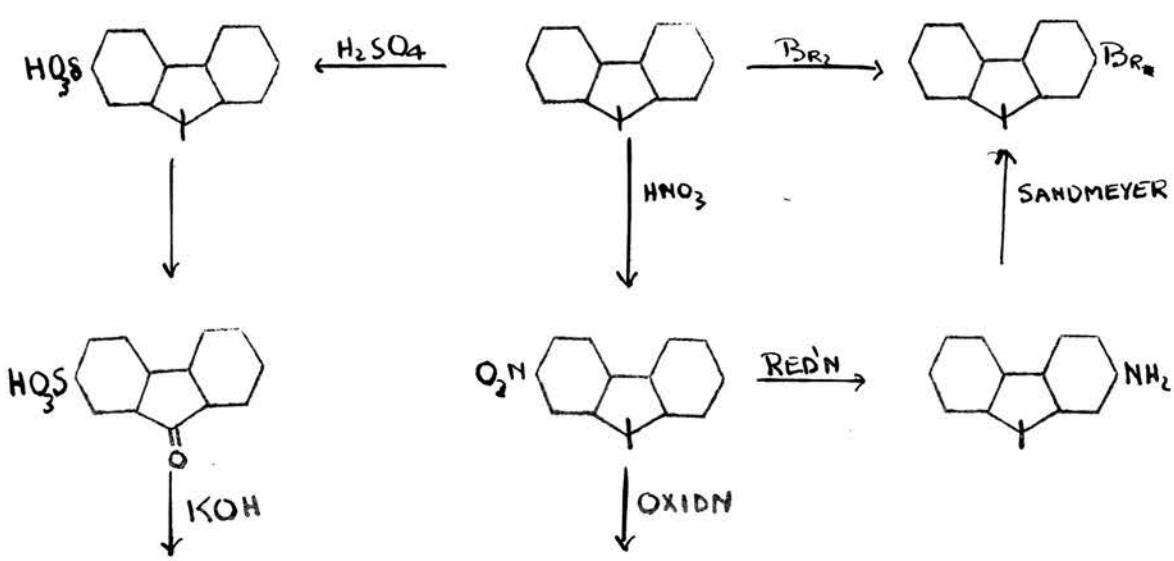
(ii) Bromine reacts with fluorene giving 2-bromofluorene and 2:7-dibromofluorene (Clarkson and Gomberg, J.A.C.S., 1930, 52, 2881).

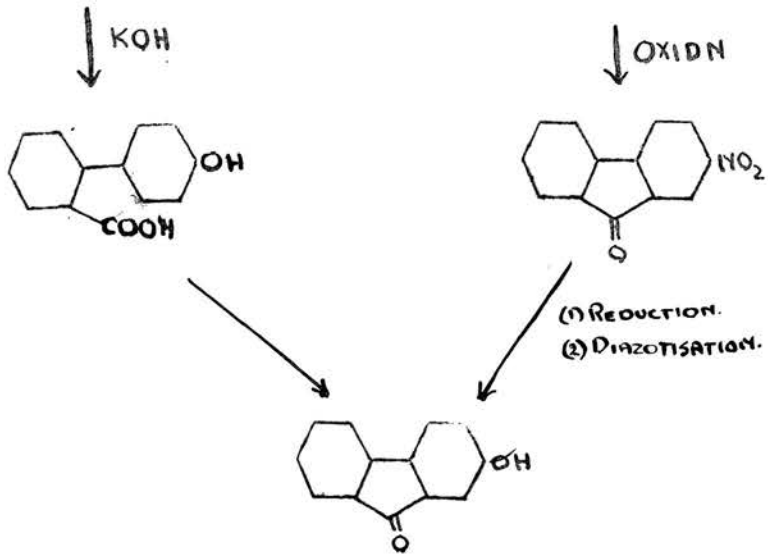
(iii) Nitration gives the 2-nitrofluorene (see page 260) in excellent yield (Diels, Ber., 1901, 34, 1758).

(iv) Sulphonation gives the 2-sulphonic acid (Wedekind and Stüsser, Ber., 1923, 56, 1561).

The inter-relationships of these monosubstituted derivatives were convincingly demonstrated by Courtot (Ann.chim., 1930, [10], 14, 5-146). The essential basis is shown below in Scheme 14.

SCHEME 14

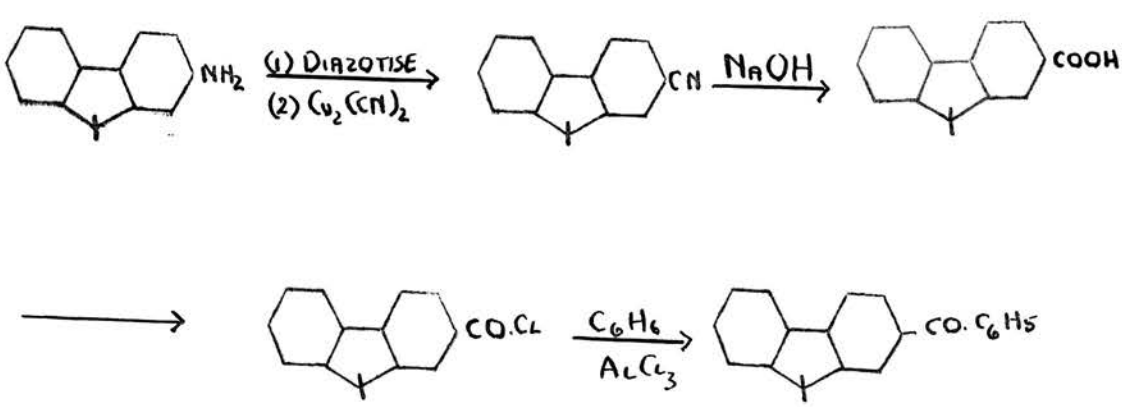




The orientation has been completed by syntheses (e.g. of 2-aminofluorene, Strassbourger, Ber., 1884, 17, 107) of several of the 2-monosubstituted fluorenes and fluorenones. These syntheses are discussed in Section III.

(v) Fortner (Monatsh., 1904, 25, 443) showed that the monobenzoyl fluorene obtained by the Friedel Crafts reaction was the 2-isomer by identification with the synthetic product from 2-aminofluorene by the Scheme 15.

SCHEME 15



Dziewonski and Schayer (Abs., 1931, 25, 5416) oriented the mono-acetyl fluorene by Beckmann transformation of the oxime to give 2-acetamidofluorene.

In mono-substitution fluorene has been shown to be reactive in the 2-position. There is one exception claimed however, namely, mercuration. Some work on this has been described in Part II (page 257). The apparent "anomaly" of mercuration is discussed below and the conclusions of Part II are used, but details are given in the later section.

The Mercuration of Fluorene

Goswami and Das Gupta (Abs., 1932, 26, 445) reported the formation of fluorene mercurichloride by treating fluorene with mercuric acetate in boiling acetic acid solution and then converting the acetate to the chloride by treatment with alcoholic calcium chloride. These Indian workers did not orientate their product.

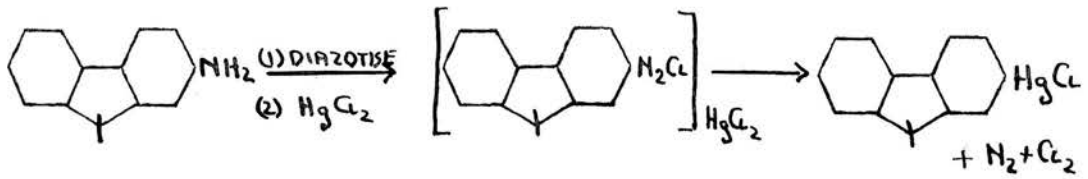
G.B. Bachman and Miller (J.A.C.S., 1935, 57, 2447) could not repeat the work of Goswami and Das Gupta in so far as the physical characteristics of the products differed. They prepared the mercurichloride as before by treating fluorene mercuriacetate with calcium chloride, but they obtained the mercuriacetate by two procedures.

(1) The first was essentially that of Goswami and Das Gupta. Bachman and Miller treated the derived mercurichloride with bromine and isolated in good yield, a "mono-bromofluorene", M.P. 163°C., which they oxidised to a "monobromo fluorenone", M.P. 185-7°C. This they claimed to identify with 4-bromofluorenone synthesised "unequivocally" by two procedures (cf. Section III (page 98) and Part II (page 254)).

(2) The second procedure gave a mixture of mercurichlorides, the mercuriacetate having been obtained by fusion of fluorene with mercuric acetate; Bachman and Miller claimed the isolation of two "monobromofluorenes" by treatment with bromine. The first, present in smaller quantity was 3-bromofluorene, M.P. 88-94°C., "identical" with the product, M.P. 94°C., of Clemmensen reduction of authentic 3-bromofluorenone. The fluorene on oxidation gave 3-bromofluorenone, M.P. 163°C. The second product, present in greater quantity, was 4-bromofluorene, M.P. 148-9°C., which they said was identical with the compound above which gave 4-bromofluorenone on oxidation. Very few analyses were given.

Pablo Chanussot (Abs., 1938, 32, 7030) has also investigated the mercuration of fluorene by essentially the procedure of Goswami and Das Gupta. He also isolated a product, M.P. 163°C., on brominating the mercurichloride. He states that this is evidence of abnormal substitution and claims confirmation by synthesis of the 2-mercurichloride from 2-aminofluorene

(presumably via the diazonium chloride mercurichloride).



The mercurichloride on treatment with iodine gave 2-iodofluorene. As a by-product he isolated difluorenyl mercury.

Huntress, Pfister and Pfister were the next to investigate the mercuration of fluorene (J.A.C.S., 1942, 64, 2845-9). They do not go into details of the actual mercuration but report that they could not repeat Miller and Bachman's oxidation of the compound M.P. 163°C. The importance of their paper lies in the fact that they also synthesised unequivocally 1-bromofluorenone and 4-bromofluorenone and neither of these compounds melted at 187°C. (i.e. the M.P. of 4-bromofluorenone, according to Miller and Bachman). This work when associated with the synthesis of 4-bromofluorenone by Heilbron and Hey (J., 1938, 1364-7) is strong evidence that the conclusions of Miller and Bachman regarding the process of mercuration can be completely disregarded. The "unequivocal syntheses" used by Miller and Bachman are discussed in Section III where the work of Huntress et alia and of Heillron and Hey is also described.

Interest was centred at one stage (page 248) on the synthesis of 3-bromofluorene. The possibility that the process of mercuration did in fact give the 3-mercuri-compound was therefore explored. Both methods of mercuration used by Bachman and Miller came under examination. The conclusions reached were

(1) As the products of mercuration are only separated from starting materials, the physical characteristics of the products cannot be regarded as critical evidence of large differences between the various preparations. The differences in colour are due to different degrees of purity of fluorene employed and the differences in melting points are probably due to different degrees of mercuration with perhaps the production of isomeric mercuri-compounds. The melting point was found to be a very poor indication of purity as the mercuri-compounds darken and sinter before melting.

(2) The bromination of the mercuri-compounds invariably gave a mixture of the following composition:

(i) fluorene
(ii) a bromofluorene, M.P. 163°C.
(iii) other bromofluorenes
(iv) unchanged starting material
(v) a bromofluorene mercuribromide
(vi) polybromofluorene mercuribromides
(vii) other products.

(i) The starting material contained no fluorene and hence the fluorene must have been produced from the fluorene mercuri-chloride.

(ii) The compound, M.P. 163°C., had properties similar to that of Bachman and Miller but is a dibromo-compound. It is not 2:7-dibromofluorene (M.P. 163°C., Mixed M.P. 145-50°C.) and it gives a dibromofluorenone, M.P. 139.5°C., in excellent yield on oxidation.

(iii) There were other bromofluorenes present which could not be separated, but there was no evidence of the presence of a monobromofluorene.

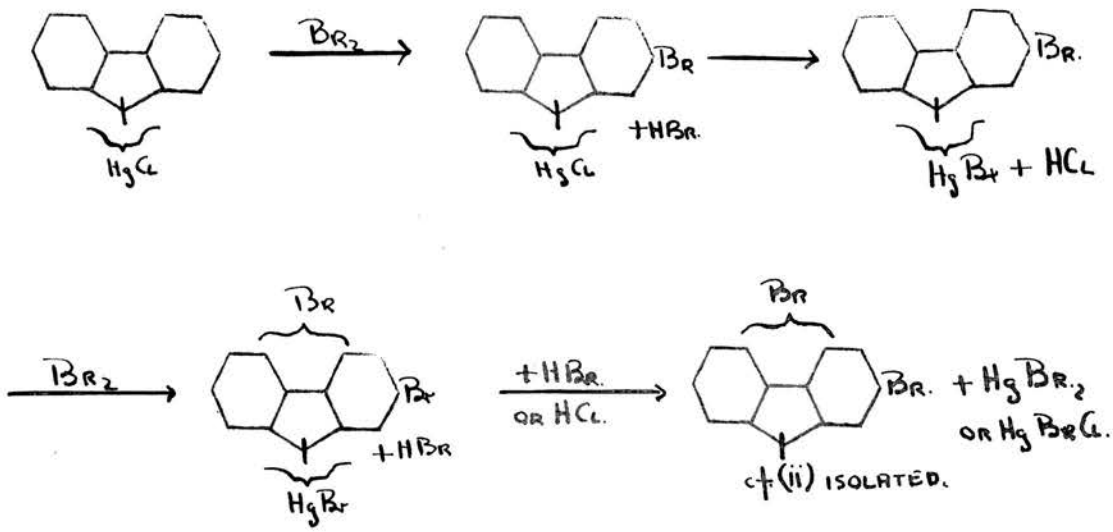
(iv) There was much insoluble material left which contains mercury and it probably contained starting material for only one mole. of bromine was used.

(v) A mercury compound containing ~~two~~ 3 atoms of bromine per mole. was isolated in a fair state of purity.

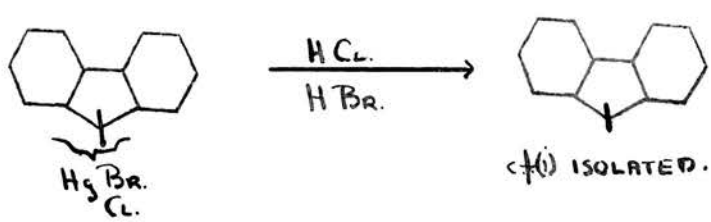
(vi & vii) There was present much insoluble material and it is probable that polybromination occurred. There were also some insoluble tarry products.

From this the scheme of reaction (16) was suggested on the assumption that the mercuri-compound was a mono-mercuri-compound.

SCHEME 16



ALSO



The most significant fact is that of all the mercuri-halogeno-compounds encountered the ~~mono~~di bromofluorene mercuri-bromide which was isolated was by far the most soluble. This would favour further bromination. It is also suggested that the removal of mercury from the mercuricompounds was by reaction of the mercuricompounds with acid rather than free halogens for mercurichlorides are sensitive to acids, i.e.

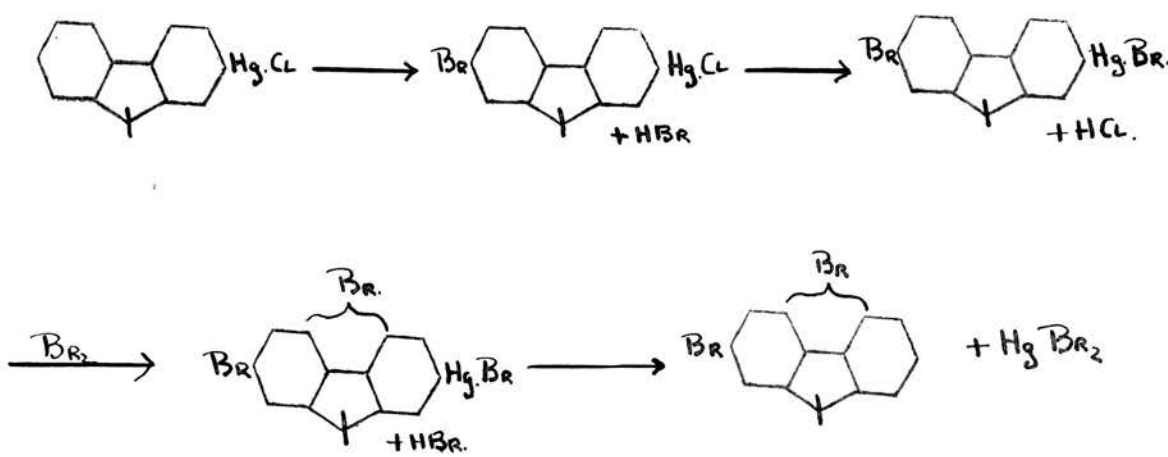
$$R.Hg.X + HX \longrightarrow RH + HgX_2 \quad \ldots\ldots\ldots (1)$$

Rather than $$R.Hg.X + X_2 \longrightarrow R.X + HgX_2 \quad \ldots\ldots\ldots (2)$$

This is in agreement with the production of fluorene which could not be produced by mechanism (2).

In this scheme there is no reason why mercuration should not occur in position 2, of the fluorene nucleus and the bromination follow thus, Scheme 17.

SCHEME 17



It is patent, however, that, if the work of Chanussot is correct, then this mechanism is incorrect. It is unfortunate that only an abstract of his paper is available, for it is inconceivable that he prepared the 2 fluorene-

mercurichloride if the abstract is correct. According to it, Chanussot prepared the mercurichloride from the diazonium chloride by reaction with mercuric chloride; this could give rise only to the diazonium chloride mercurichloride. The formation of anylmercurichlorides requires the presence of copper powder to effect the reduction of the aryldiazonium chloride mercurichloride (cf. Saunders, "The Aromatic Diazo Compounds", Arnold 1947). The scheme of reaction is

$$\overline{Ar}.N_2Cl + HgCl_2 \longrightarrow \overline{Ar}.N_2.HgCl_3.$$

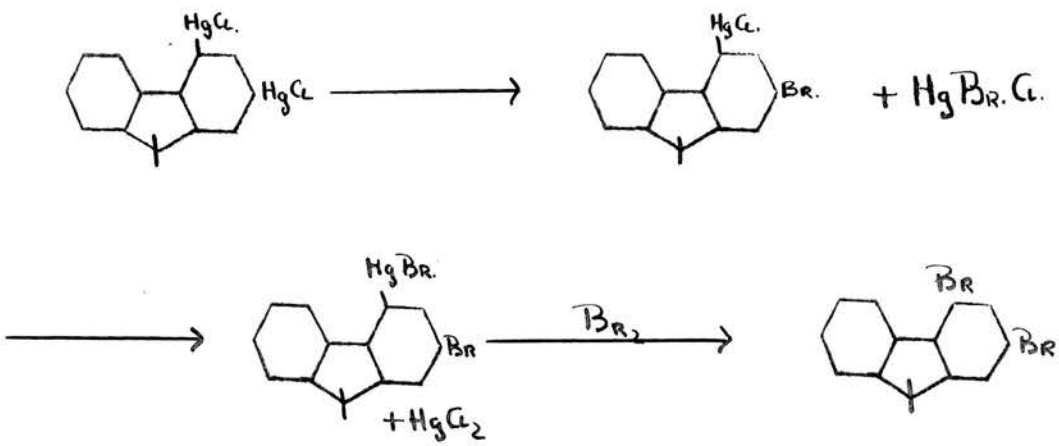
$$\overline{Ar}.N_2.HgCl_3 + \boxed{2Cu} \longrightarrow \overline{Ar}.HgCl + N_2 + 2CuCl$$

No mention of copper powder is made in the abstract. Although the reaction of the compound with iodine to give 2-iodofluorene is consistent with Chanussot's formulation, it is not altogether inconsistent with its formulation as the aryldiazonium chloride mercurichloride which may well react with iodine to give 2-iodofluorene (cf. Saunders, loc.cit., 291).

If investigation substantiates Chanussot's work in the future, then mercuration may be conceived as occurring other than in the 2-position. The whole matter is however fraught with difficulty and would require intensive study. The principal difficulty is that no mercuration product so far made can be said to be pure, as analyses have not been made

or purification even effected. The bromo-compounds obtained have been shown (Part II) to be di-bromo-compounds, so if Chanussot's claims are tenable another possibility must be considered, namely that the di-bromo-compound, M.P. 163°C., arises from a dimercurichloride, thus Scheme 18.

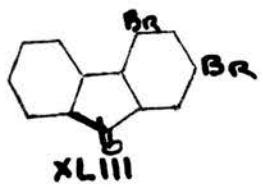
SCHEME 18



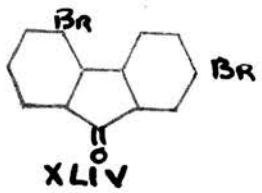
The bromomercuribromide isolated would then be an intermediate in the decomposition of the mercuri-compound, rather than a substitution product of the mercuri-compound.

The dibromofluorenone, M.P. 139·5°C., derived from the dibromofluorene, M.P. 163°C., may be identical with the dibromofluorenone, M.P. 133°C., which has been isolated by distilling impure 4:4'-dibromodiphenic acid with chalk (Claus and Erler, Ber., 19, 3156; Goldschmiedt and Schranzhofer, Monatsh., 1895, 16, 820). The principal product was the 2:7 isomer. The impurities present in the 4:4'-dibromodiphenic acid would

most probably be the 2:4'-dibromo or the 2:4 dibromo-isomer in which case the fluorenone, M.P. 133°C., would be XLIII or XLIV



XLIII



XLIV

Now XLIV is known (Courtot and Moreaux, Compt Rend., 217, 453-4) and it melts at 181°C. This would reduce the possibilities to XLIII.

The matter is, however, complex and the problem would be capable of solution only after much study and after the synthesis of several dibromofluorenones had been achieved. The problem of mercuration must at present be left over, but should not, until further evidence is sought, be accepted as evidence of abnormal substitution.

Disubstitution. This is considered from two viewpoints

(1) Substitution reactions that may occur in any position in the nucleus relative to the first substituent.

(2) Substitution reactions which must take place in a position ortho to the first substituent.

(1)

(i) The bromination of fluorene gives in addition to 2-bromofluorene, 2:7-dibromofluorene. This is the only nuclear dibromo-compound prepared by direct bromination. The structure was shown by the synthesis of the oxidation product, 2:7-dibromofluorenone, from 2:7-dibromophenanthroquinone by the method of Schmidt and Bauer (Ber., 1905, 38, 3753; see Section III, page 113).

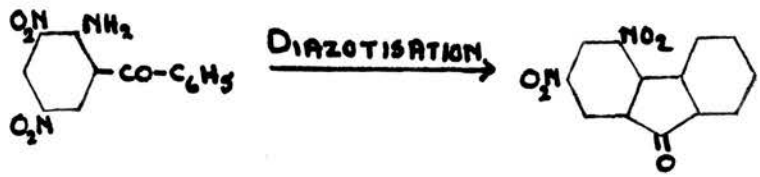
(ii) The nitration of 2-bromofluorene gives a product identical with that of bromination of 2-nitrofluorene (Courtot, loc.cit.). The identity of the 2-and 7-positions necessitates that the disubstitution should be assigned the 2-and 7-positions. The 2-bromo-7-nitrofluorene was converted through 2-bromo-7-nitrofluorenone and 2-bromo-7-aminofluorenone into 2:7-dibromofluorenone.

(iii) The sulphonation of 2-nitrofluorene gives the 7-sulphonic acid for reduction and deamination yields fluorene-2-sulphonic acid (Courtot, loc.cit.).

(iv) The nitration of 2-nitrofluorene gives a mixture of 2;7-dinitrofluorene (66%) and 2;5-dinitrofluorene (22%)

(Antakrishnan and Hughes, J., 1935, 1607). The structure of the 2:7-isomer was shown by the synthesis of the corresponding fluorenone by the Schmidt and Bauer method (Ber., 1905, 38, 3744) from 2:7-dinitrophenanthraquinone. As this dinitrophenanthraquinone is the key to the synthesis of all the 2:7-disubstituted fluorenones its orientation is important. Schultz (Ann., 1879, 196, 31) converted it first to the 2:7-diaminophenanthraquinone, then to 4:4'-diamino-2-2'-diphenic acid which on decarboxylation gave the well known 4:4'-diamino biphenyl.

The structure of the other isomer was shown by Morgan and Thomason (J., 1926, 2691) to be either the 2:4 or 2:5-compound and they preferred the latter formulation. Their evidence was based on the synthesis of 4-nitrofluorenone, by the Schmidt and Bauer procedure, from 4-nitrophenanthraquinone. This on nitration gave a compound identical with the fluorenone derived by oxidation of the isomer isolated from the nitration of 2-nitrofluorene. They considered that it would be improbable for dinitration to occur in the one ring so they gave the product the 2:5-structure. Ullmann and Broido (Ber., 1906, 39, 360) had however effectively completed this work for they had synthesised 2:4-dinitrofluorenone from 2-amino-3:5-dinitrobenzophenone by the Ullmann fluorenone synthesis (Section III, page 107) and this was different from the product of direct nitration.



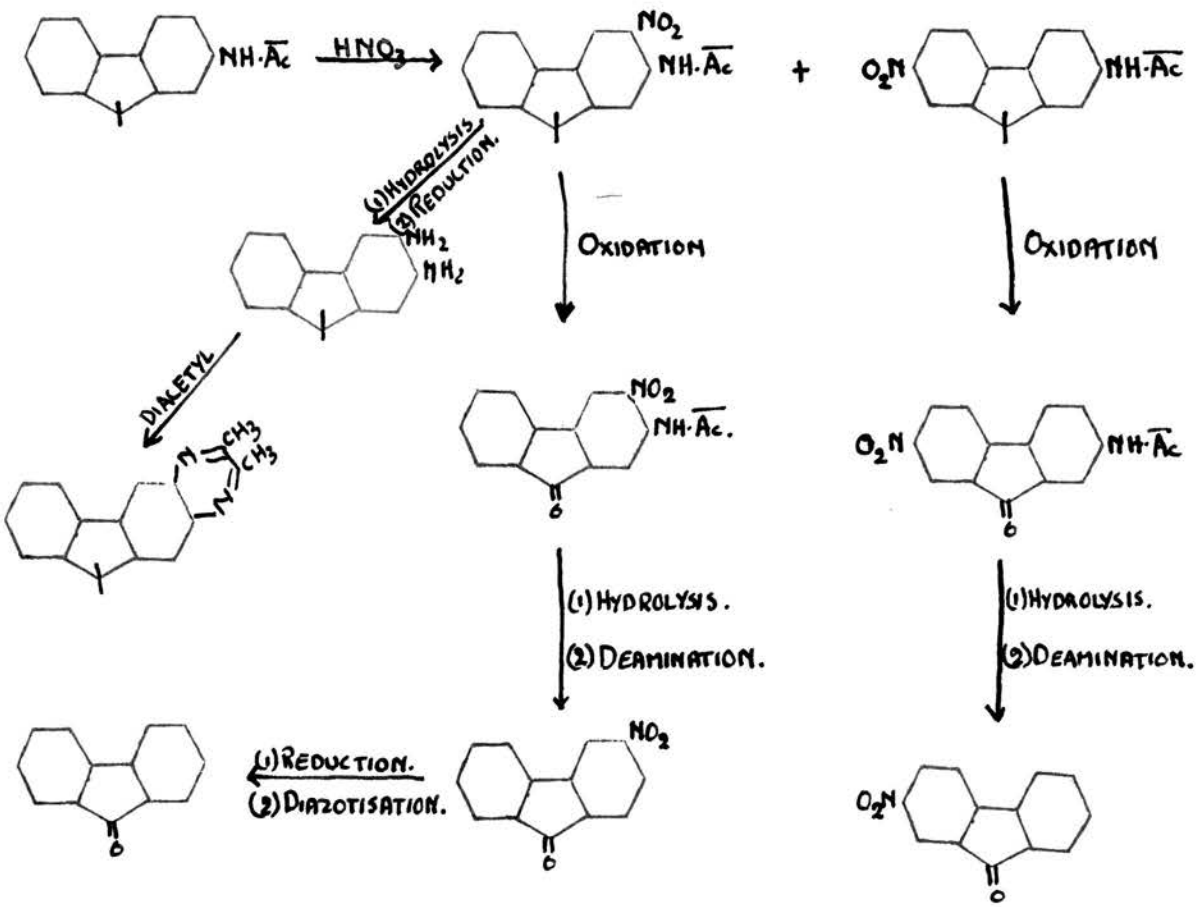
(v) In the Friedel Crafts reaction diacetylation has been shown to give 2:7-diacetylfluorene, for rearrangement of the dioxime gives 2:7-diacetamidofluorene and oxidation gives fluorenone-2:7-dicarboxylic acid (Dziewonski, Kuzdrazl, and Mayer, Abs., 1935, 29, 1084). An isomeric diacetyl fluorene isolated by Dziewonski and Klesgcz (Abs., 1933, 27, 283) formed a dioxime which on Beckmann rearrangement gave a diacetamidofluorene. They claim that the diaminofluorene obtained on hydrolysis is identical with the orthodiamine obtained by Diels, Schill and Tolsen (Ber., 1902, 35, 3284). This diamine is the 2:3-isomer (Eckert and Langecker, J.Prakt.Chem., 1928, 118, 263). It is again unfortunate that this paper is only available as an abstract for there is no indication that they did, or did not do, mixed melting points. Their diacetyl derivative of the diamine is not a suitable derivative as it has not been prepared by any of the other workers. A much more characteristic derivative would have been produced by condensing with diacetyl or phenanthraquinone (Diels, et alia, loc.cit., and

Eckert and Langecker, loc.cit.). If their work is repeated it might be advantageous to oxidise the diacetyl fluorene to the corresponding fluorenone diacid for fluorenone-2:3-dicarboxylic acid has recently been synthesised (Lothrop and Coffman, J.A.C.S., 1941, 63, 2564). Until this work has been re-examined it must be treated with reserve, for substitution in a position ortho to an acetyl group is unusual when other directing influences are not involved. It should be pointed out, however, that the most probable alternative, 2:5-diacetylfluorene, would apparently not be acceptable for the physical characteristics of the derived diamine and diacetamidofluorene are not in accord with those for the known 2:5-isomers.

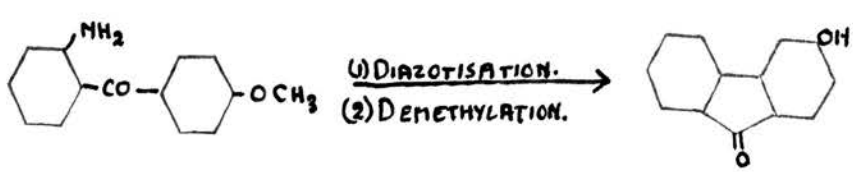
(vi) The sulphonation of 2-aminofluorene gives the 7-sulphonic acid as deamination gives the 2-sulphonic acid.

(vii) Nitration of 2-acetamidofluorene gives a mixture of 3-nitro-2-acetamidofluorene and 7-nitro-2-acetamidofluorene. The structure of these isomers was proved by deamination after oxidation to the corresponding fluorenones. The products were 2-nitrofluorenone and 3-nitrofluorenone. The former is known and the latter was identified by conversion via 3-aminofluorenone to 3-hydroxyfluorenone (Eckert and Langecker, loc.cit.). The original 3-nitro-2-acetamidofluorene had been hydrolysed and reduced to an ortho diamine and the assignation of the above structure is therefore justifiable.

SCHEME 19



This work depended on the structure of 3-hydroxyfluorenone being known. The latter compound was synthesised by the Ullmann method from 4-methoxy-2'-aminobenzophenone (see Section III) (Ullmann and Bleier, Ber., 1902, 35, 4278).



The 1-hydroxy compound had been prepared by Staedel again by a variation of the Ullmann method (Ber., 1895,28,111-113) from 2-amino-2'-aminobenzophenone. The identification of the 3-hydroxy fluorenone was complete.

(ix) The bromination of 2-acetamidofluorene gives the 7-bromo-2-acetamidofluorene (Bell and Mulholland,J.,1949, 2021; J. Campbell, Anderson and Gilmore,J.,1940,450). The bromination of 2-N-tosylaminofluorene in pyridine gives the 3-bromo-2-N-tosylaminofluorene (Bell and Mulholland loc.cit). They justify their designation of structure by showing that further bromination gives a product which when hydrolysed is identical with that obtained by hydrolysis of the product of bromination of 2-acetamidofluorene and designated as the 3:7-dibromoacetamidofluorene. They also claim that a small amount of the 1-bromo-2-tosylaminofluorene is produced on bromination in pyridine.

The whole matter of the bromination of 2-aminofluorene derivatives is discussed in the Section on polysubstitution.

(β). Disubstitution which must involve an ortho position to the primary substituent is considered from three viewpoints:

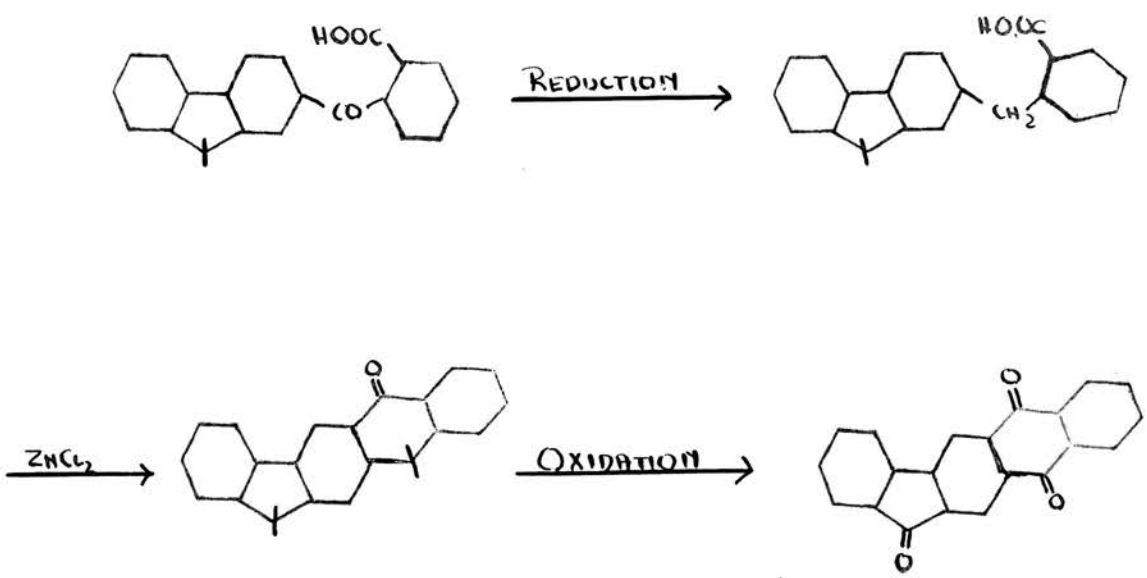
(i) Intramolecular acylation.

(ii) Reactions of 2-aminofluorene, e.g. Skraup synthesis.

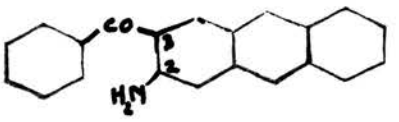
(iii) The Pschorr synthesis (cf. Cook, J., 1949, 850).

(i) Goldschmiedt and Lipshitz (Monatsh., 1904, 25, 1164) reacted phthalic anhydride with fluorene in the normal manner and obtained 2-fluoryl-o-benzoic acid. The cyclisation of this acid has been studied by Dansi and Semprorý (Gazz., 1933, 63, 681) but most effectively by Barnett, Goodway and Watson (Ber., 1933, 66, 1879). The latter workers demonstrated by scheme 20 that cyclisation occurs in the 3 position.

SCHEME 20

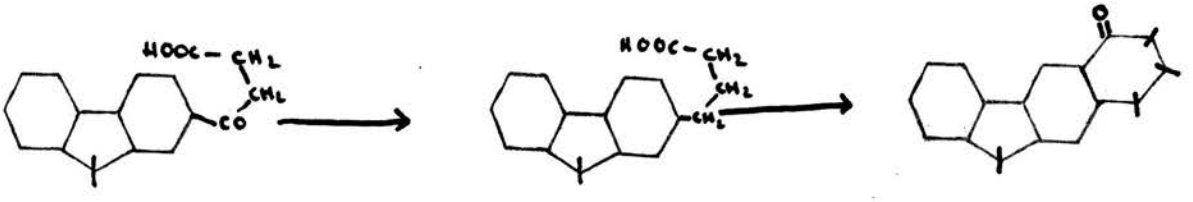


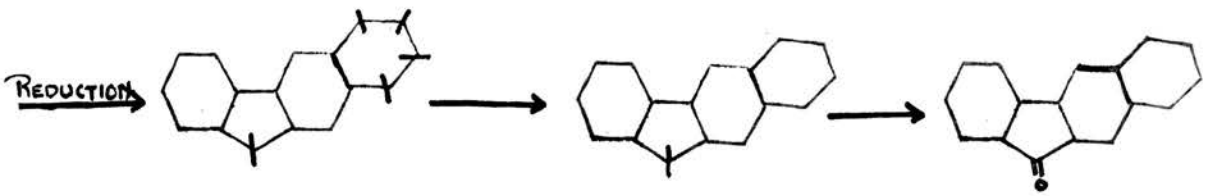
The resulting 1-keto-2:3-indeno-2':3'-anthraquinone had been synthesised by the Ullmann procedure (Ullmann and Dasgupta, Ber., 1914,47,553) from 2-amino-3-benzoylanthraquinone.



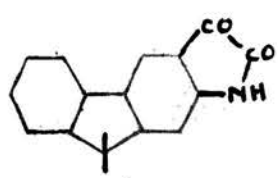
Koelsch (J.A.C.S., 1933,55,3885) also identified the position of cyclisation of fluorene-2:γ-butyric acid as the 3-position. The butyric acid was obtained in the normal manner i.e. from the reduction of the succinoylation product of fluorene. The cyclisation was effected via the acid chloride with aluminium chloride in 45% yield. Reduction of the indeno-tetralone to the tetralin followed by dehydrogenation gave the known 2:3-benzofluorene. This was further oxidised to the 2:3-benzofluorenone (Scheme 21).

SCHEME 21

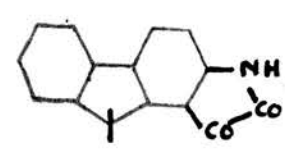




(ii) 2-aminofluorene has been shown to undergo the Skraup synthesis in a unidirectional manner (Diels and Staehlin, Ber., 1902, 35, 3275). The exact orientation has not been worked out in this case or in any of the subsequent applications of similar syntheses (Hughes, Lions and Wright, J.Proc.Roy.Soc. New South Wales, 1938, 71, 449; Loevenich and Loeser, J.Prakt. Chem., 1929, 122, 285; Fel'dman, Abs., 1937, 31, 1407). Hughes, Lions and Wright, however, tacitly assume the 1-orientation in preference to the 3-orientation but the basis of their assumption does not bear examination. Recently Neish (Rec., 1948, 67, 349) has applied a synthetic method of Martinet (Compt. Rend., 1913, 156, 1625 etc.) to 2-aminofluorene and obtained eventually an indenoisatin, (a) or (b) below.

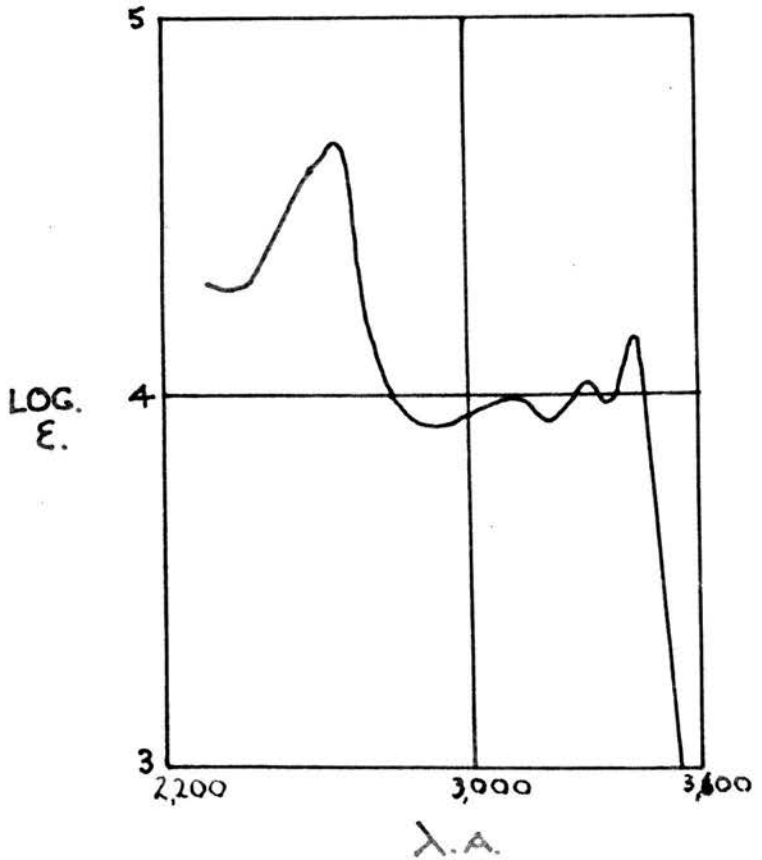


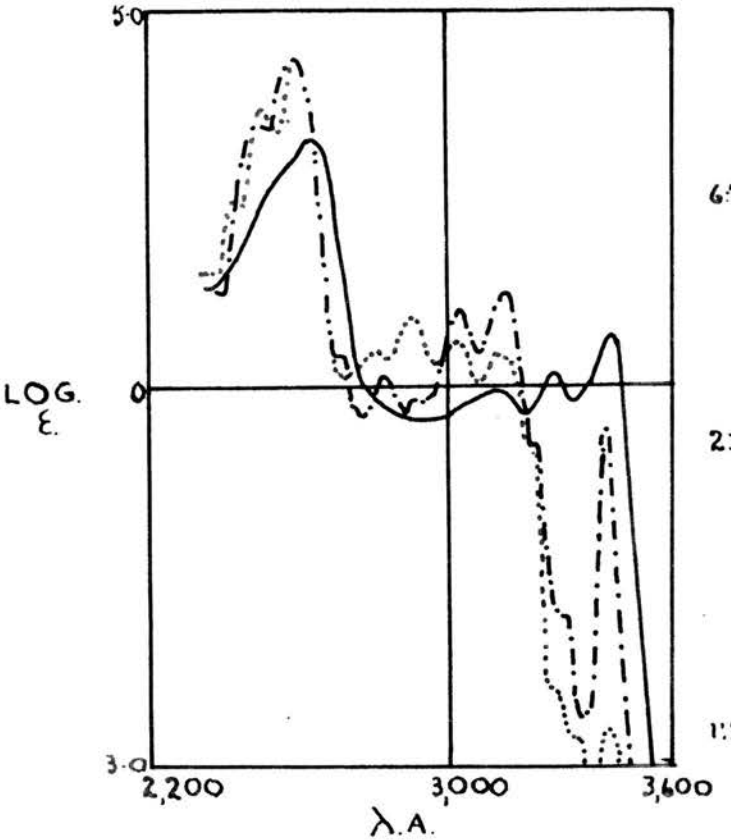
(a)

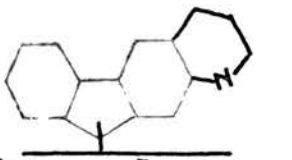


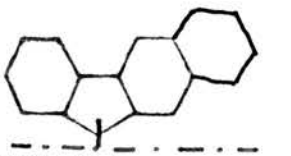
(b)

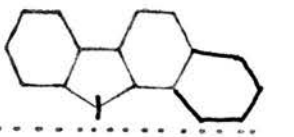
V






6:7:[2':2':INDENO]QUINOLINE


2:3 BENZO FLUORENE

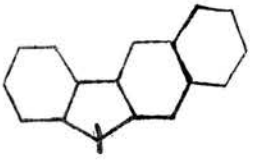

1:2 BENZOFLUORENE.

λ.MAX.	LOG. ε.
3,425	4·14.
3,280	4·02
3,100	3·99
2,650	4·66

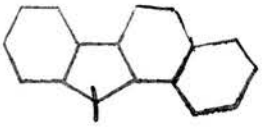
λ.MIN.	LOG. ε.
3,365	3·95.
3,210	3·89
2,960	3·93
2,350	4·25

In Part II, Section II, it is shown by degradation that the product is in fact (a). This means that cyclisation occurs preferentially in the 3-position. The absorption spectrum of the indenoquinoline of Diels and Staehlin has also been examined.

In Fig. V, opposite, it is contrasted with the absorption curves of the two indenonaphthalenes a' and b'



(a')

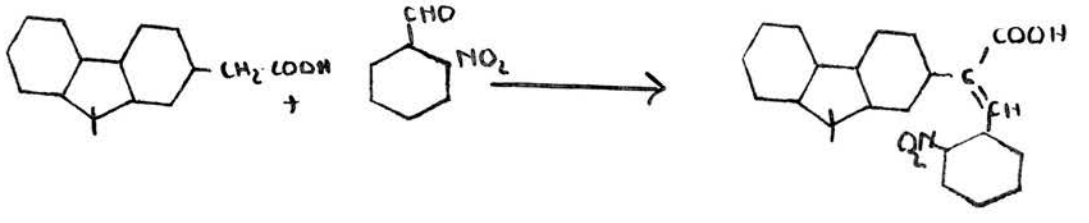


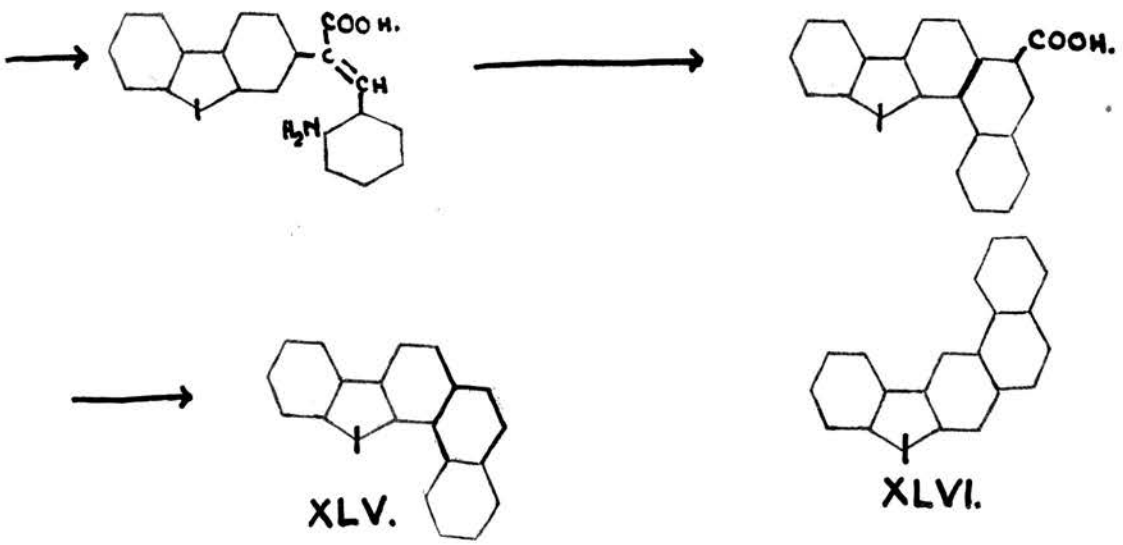
(b')

It is apparent that the absorption curve of the indenoquinoline resembles that of (a') rather than that of (b'). It is apparent from this that cyclisation in the 3-position has probably occurred in the Skraup reaction.

(iii) Cook and Stephenson (loc.cit.) carried out the series of reactions shown in Scheme 22.

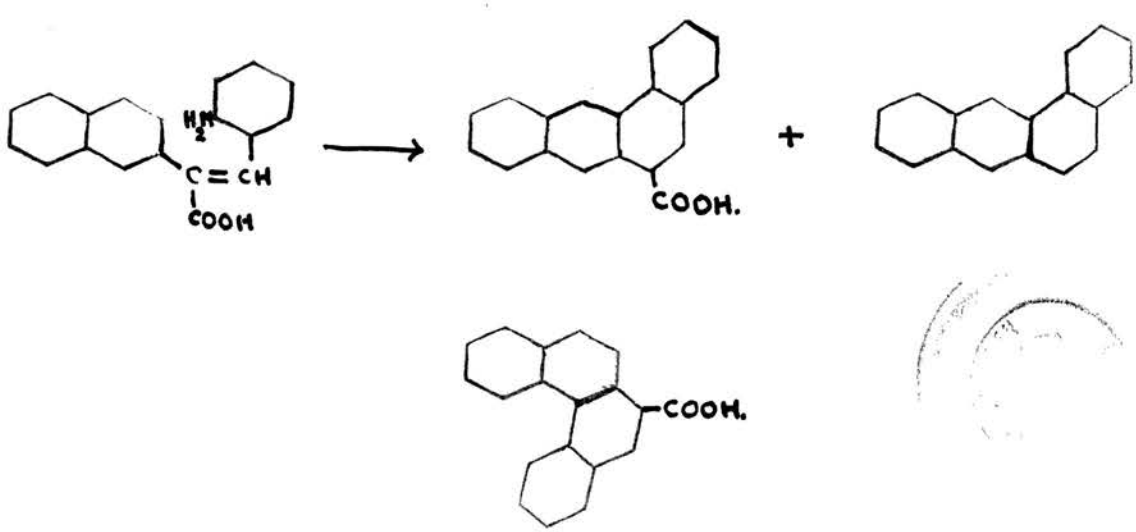
SCHEME 22





Instead of 2:3-indeno-2':3'-phenanthrene, XLVI, the expected product, they obtained 2:3-indeno-4':3'-phenanthrene, XLV. Cyclisation must have occurred in the 1-position in preference to the 3-position. Although this is surprising it is not unparallelled for Cook (J., 1931, 2524) carried out a similar sequence of reactions with β-naphthylacetic acid and here obtained a mixture Scheme 23.

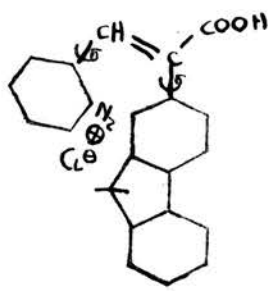
SCHEME 23



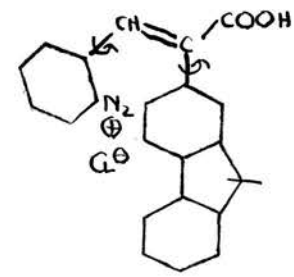
In the naphthalene series a greater proclivity for unidirectional cyclisation exists than in the fluorene series. The fact that a mixture is produced in the naphthalene series in a cyclisation of a β-derivative would make the production of a mixture in an equivalent reaction of the fluorene series less surprising. Cook and Stephenson did in fact obtain a mixture at the cyclisation stage but the acid leading to XLV was the only one present in quantity.

The Pschorr synthesis has two added factors to be considered.

(1) It is known that the cis disubstituted acrylic acids are necessary if cyclisation is to be effected.



A.



B.

Although unrestricted rotation of groups about a carbon to carbon single bond is accepted, it is in fact an ideal condition. There will be in such complex cases as above certain relative positions of the substituent groups of the acrylic acid structure which are potentially preferable and it appears that in the case of the Pschorr synthesis the relative positions

favour cyclisation in the 1-position rather than the 3-position. Reaction in the 1-position rather than the 3-position in this case, probably indicates that a decisive factor is the difference in potential energies of the two structures (A) and (B), above, which would respectively yield 1- and 3-substituted products.

(2) To this must be added the directive influence of the diazonium group or its initial decomposition product which can act through a conjugated system and influence the fluorene group in the molecule.

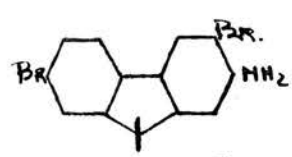
Whether these factors together are responsible for the direction of cyclisation or whether only one is responsible cannot be decided without further investigation.

Polysubstitution of Fluorene and Fluorenone

Schmidt and Bauer (Ber., 1905, 38, 3758) nitrated fluorenone and obtained a trinitroderivative. Bell (J., 1928, 1990) obtained an identical product by further nitration of 4-nitrofluorenone and concluded that the trinitrofluorenone was substituted in the 2,4 and 7-positions. The tetranitrofluorenone also obtained by Schmidt has, in view of Bell's work, been assigned the 2;4;5;7-tetranitrofluorenone structure.

The bromination of 2-acetamidofluorene, 2-tosylaminofluorene and 2-aminofluorene hydrochloride has been studied

(Campbell, Anderson and Gilmore, loc.cit.; Bell and Mullholland, loc.cit.; Eckert and Langecker, loc.cit.). The very readily obtained dibromo-2-aminofluorene was given the 3;7-dibromo-2-aminofluorene Structure, XLVII, by Campbell, Anderson and Gilmore in analogy with the nitration of 2-acetamidofluorene. Bell and Mulholland state that the 1-position can also be substituted and they claim the isolation of 1:3-dibromo-2-tosylaminofluorene. The latter workers, however, have not attempted any degradations which might lead to the confirmation of the suggested structure. The whole matter of the bromination of 2-aminofluorene and its derivatives is unsatisfactory; beyond the analogy of the formation of the 3:7-dibromoderivative and the nitration of 2-acetamidofluorene no suppositions as to structure can legitimately be made because of the limited experience of the availability of the 1-position in fluorene for reaction.



XLVII.

Fluorenone Substitution

In all the work described the emphasis has been placed on the substitution reactions of fluorene. Most of what has been said also applies to fluorenone. The keto group reduces the reactivity of fluorene but does not alter effectively the

positions adopted by the substituents. The parallel between the reactions of fluorene and fluorenone is made obvious by the ready interconversion of the substituted fluorenones and fluorenes for the oxidation of fluorenes to fluorenones and the reverse reduction are readily brought about.

Dihydrophenanthrene

The substitution reactions are considered under the headings:

(A) Monosubstitution in the biphenyl-like nucleus

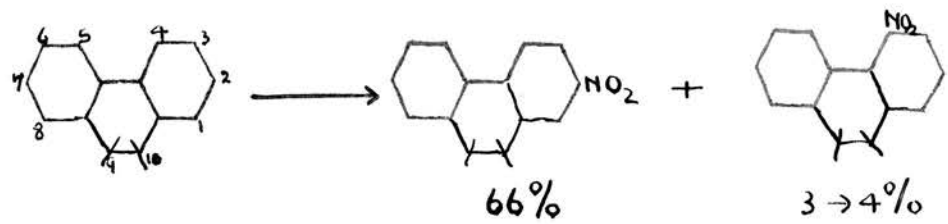
(B) Di " " " " " "

(α) involving any position with respect to the primary substituent

(β) involving an ortho position to the primary substituent

(C) Polysubstitution

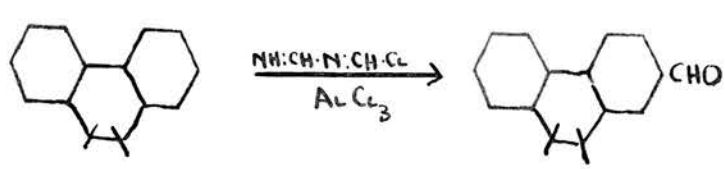
A. (i) Mosettig and Krueger (J.Org.Chem., 1938, 3, 340) have shown that nitration gives a mixture of 66% 2-nitrodihydrophenanthrene and 3-4% of the 4-nitro-isomer. (Yields are of pure material isolated.) The reaction conditions were similar to those for fluorene. The structures were demonstrated by conversion via the corresponding amines to the phenols, which were dehydrogenated and compared with the known 2- and 4-hydroxyphenanthrenes.



(ii) Sulphonation (Mosettig and Stuart, J.A.C.S., 1939, 61, 1-7) gives the 2-sulphonic acid. This was identified by fusion with KOH to give the phenol and subsequent dehydrogenation to the 2-hydroxyphenanthrene.

(iii) Acetylation (Mosettig and Burger, J.A.C.S., 1936, 58, 1857) yields 2-acetyldihydrophenanthrene. This was oxidised to 2-acetylphenanthraquinone and to dihydrophenanthrene-2-carboxylic acid under different conditions. The latter was dehydrogenated to the phenanthrene-2-carboxylic acid. Mosettig and Burger (J.A.C.S., 1937, 59, 1302) converted the 2-acetyldihydrophenanthrene oxime to the 2-aminodihydrophenanthrene by Beckmann rearrangement. This was linked with (i) and (ii) above.

(iv) 9:10-dihydrophenanthrene-2-aldehyde was also synthesised (Mosettig and Burger, loc.cit.) by the procedure of Hinkel, Ayling and Morgan (J., 1932, 2793; J., 1936, 339).



Disubstitution

(α) The Friedel Crafts acetylation of 2-hydroxydihydrophenanthrene is considered in a later section on polysubstitution and the Fries Reaction.

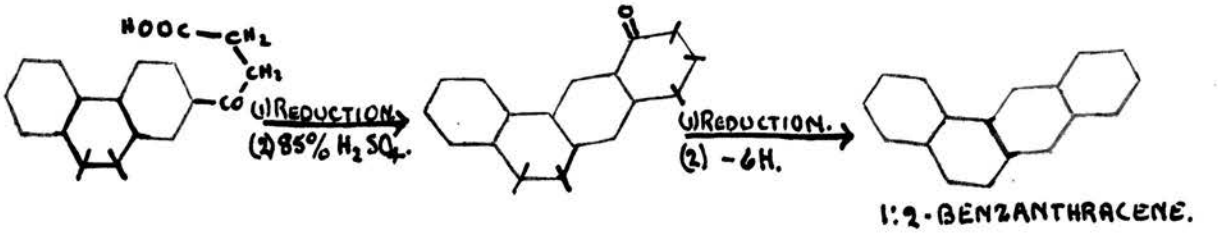
(β) Disubstitution involving the ortho position falls into two groups:

(i) intramolecular acylations

(ii) reaction of the 2-amino-dihydrophenanthrene.

(i) Succinoylation occurs in the 2-position. This was shown by synthesis from 2-acetyldihydrophenanthrene via the ω-bromoacetyl compound and sodiomalonic ester. The succinoyl compound was cyclised and the only product isolated was converted into the 1:2-benzanthracene by classical methods (thus showing that cyclisation occurred in the 3-position, Scheme 24 (Mosettig and Burger, J.A.C.S., 1937, 59, 1302)

SCHEME 24

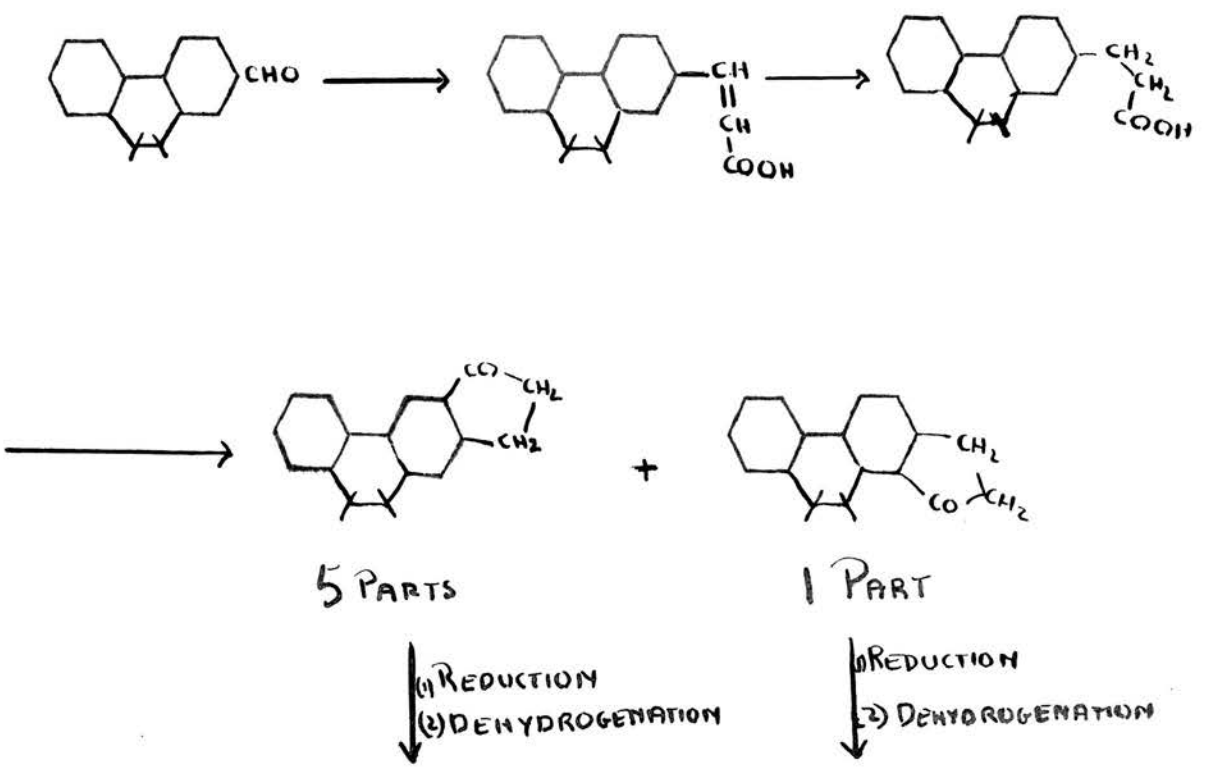


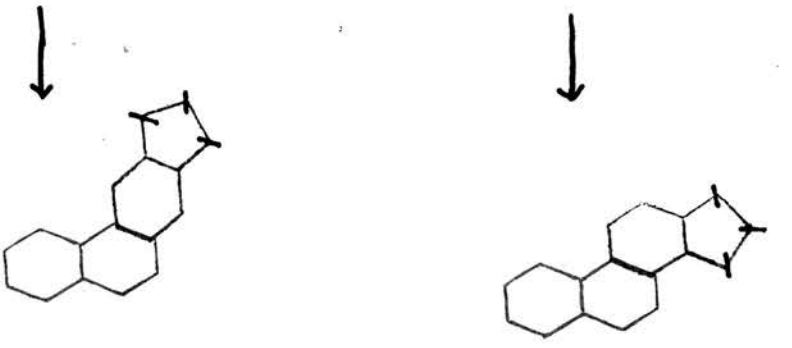
The ketone was not isolated in very good yield (cf. Haworth and Mavin, J., 1933, 1012).

Fieser and Johnson (J.A.C.S., 1939, 61, 168) cyclised the butyric acid via the acid chloride with aluminium chloride in 63% yield (pure product).

9:10-dihydrophenanthrene-2-aldehyde was converted into the acrylic acid and thence to the propionic acid. Cyclisation of the acid chloride gave two ketones in the ratio of 5:1; the reaction occurred principally in the 3-position because the cyclopentenophenanthrene derived from the product isolated in smallest yield was the well known 1:2-isomer (Scheme 25).

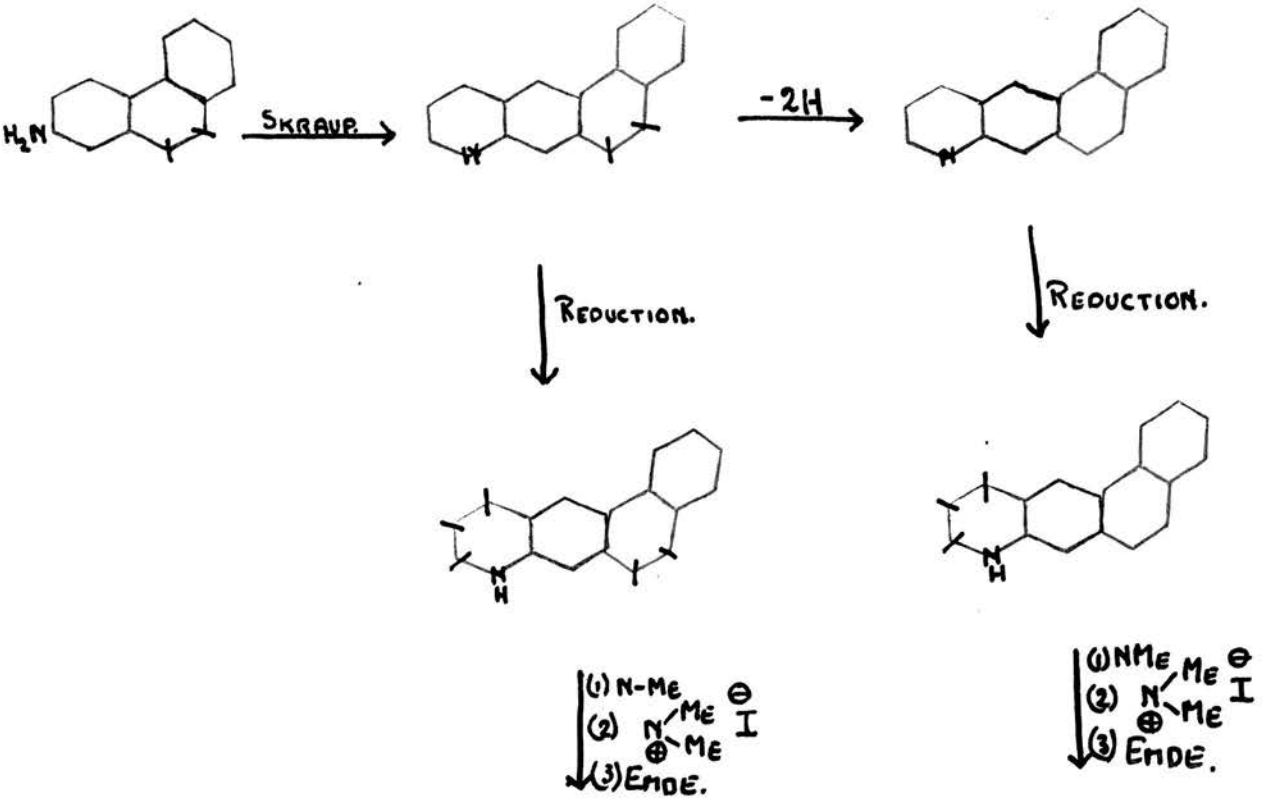
SCHEME 25

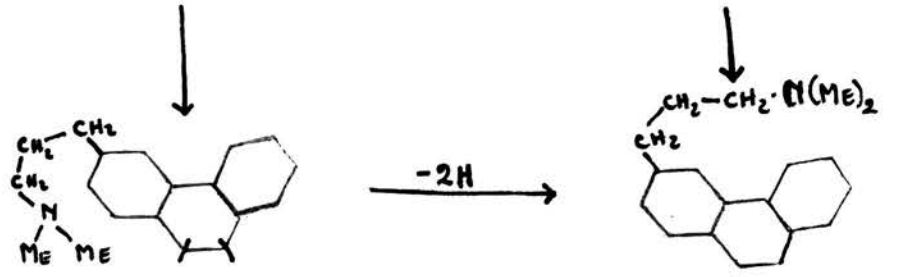




(ii) Mosettig and Krueger (J. Org. Chem., 1938,3,317-39) investigated the Skraup synthesis of certain aminophenanthrenes and of 2-amino-9: 10-dihydrophenanthrene. The method of orientation used is indicated in the case of the 2-amino-dihydrophenanthrene in Scheme 26.

SCHEME 26

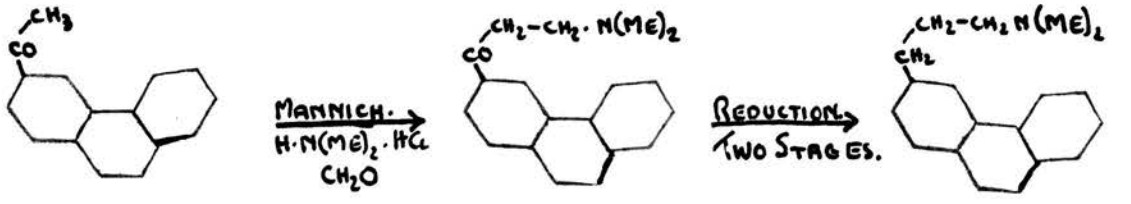




XLVIII.

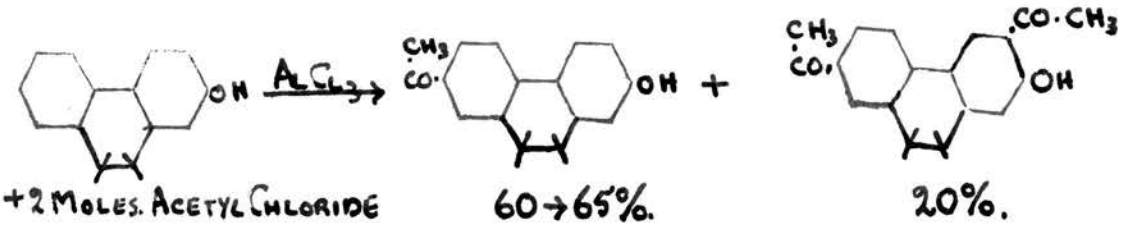
The end product (XLVIII) was synthesised from 3-acetyl-phenanthrene (Scheme 27)

SCHEME 27



The Skraup reaction afforded a 50% yield but the conditions used were different from those of Diels in 2-aminofluorene reaction (yield 80%).

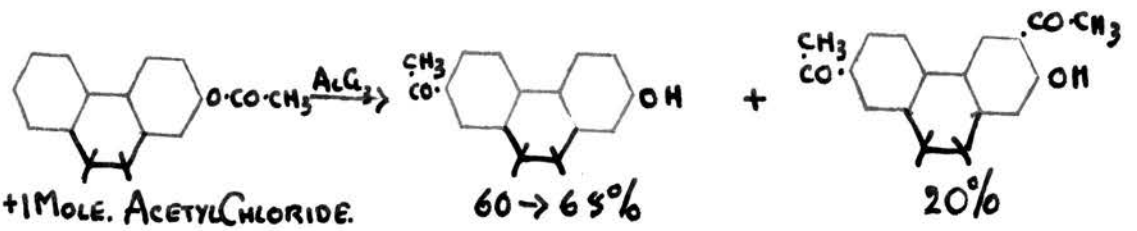
C. Polysubstitution. Mosettig and Stuart examined certain reactions of 2-hydroxy dihydrophenanthrene. They were the Friedel Crafts acetylation and the Fries rearrangement of the 2-acetoxy dihydrophenanthrene. Their results are summarised below:



+2 Moles. Acetyl Chloride

60→65%.

20%.



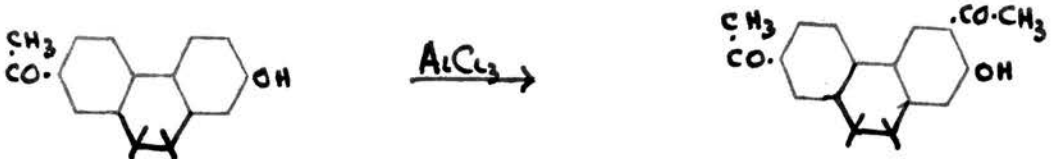
+1 Mole. Acetyl Chloride.

60→65%

20%

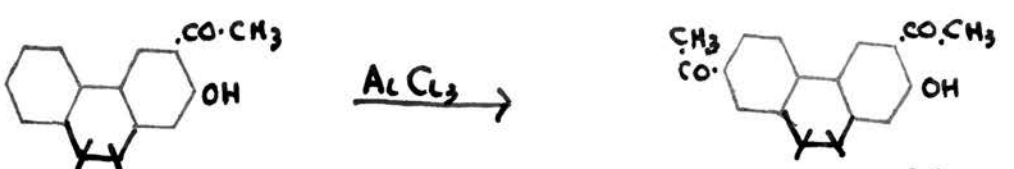
+1 Mole. Acetyl Chloride.

20% (Only Product Isolated.)



+1 Mole. Acetyl Chloride.

In Very Low Yield.



+1 Mole. Acetyl Chloride.

In Excellent Yield.

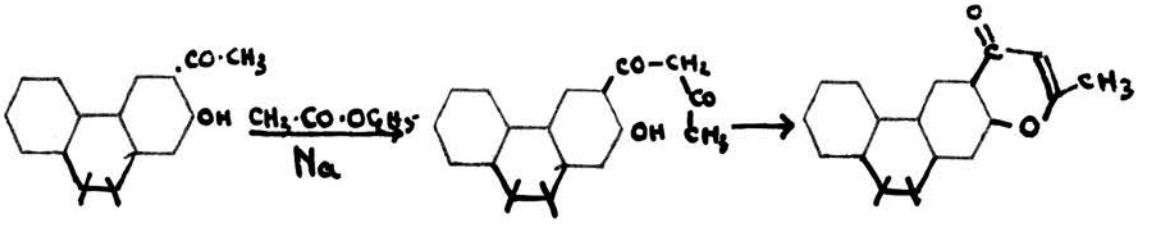
The structures of the two monacetyl compounds produced were demonstrated as follows:-

7-acetyl-2-hydroxy. This was shown by Scheme 28.

SCHEME 28

2-hydroxyl-3-acetyl. The formation of a chromone indicates the ortho hydroxy-acetyl structure (Scheme 29).

SCHEME 29



The oxidation of the 2-methoxy-o-acetyldihydrophenanthrene with hypochlorite gives the corresponding 2-methoxydihydrophenanthrene carboxylic acid which on dehydrogenation and demethylation gives a product different from the known 2-hydroxyphenanthrene-1-carboxylic acid. Hence it is the 2-hydroxy-3-phenanthrene carboxylic acid.

The structure of the 3:7-diacetyl-2-hydroxy compounds follows from the conversion of both the 7-and the 3-acetyl-2-hydroxy compound into the same diacetyl-2-hydroxydihydrophenanthrene by further acetylation.

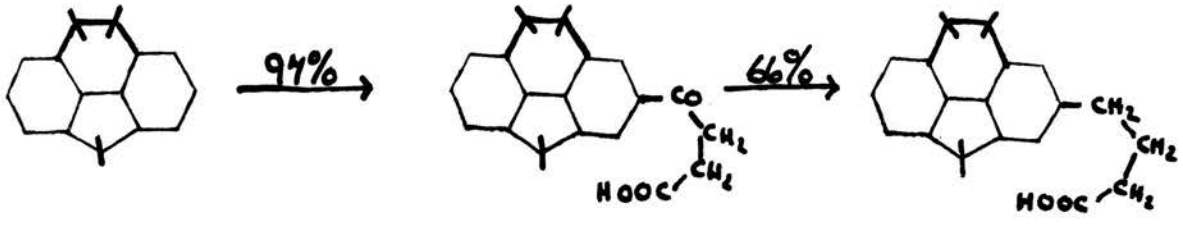
Phenanthraquinone.

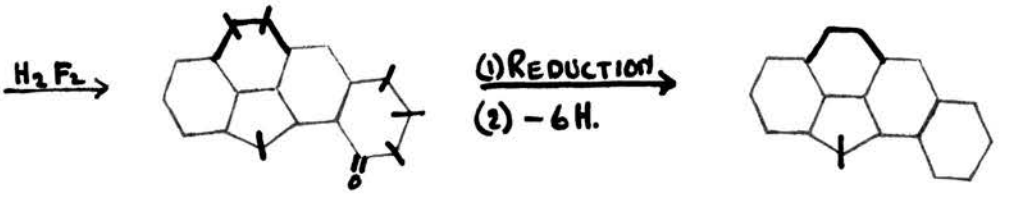
Phenanthraquinone is related to dihydrophenanthrene precisely as fluorenone is related to fluorene. Its substitution reactions resemble, in the positions adopted, those of dihydrophenanthrene, but the reactivity is much less (Everest, "The Higher Coal-Tar Hydrocarbons", Longmans, pp 312 et seq.).

The Reactions of Dihydrophenanthrindene

The succinoylation of dihydrophenanthrindene has been explored by Fieser and Cason (J.A.C.S., 1940, 62, 1294). The reaction sequence proceeds according to the following scheme 30.

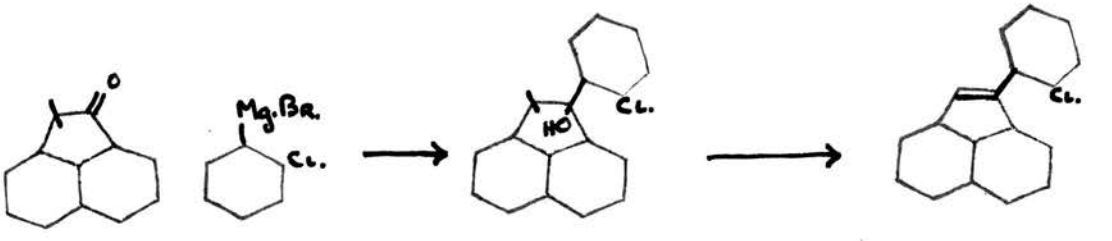
SCHEME 30

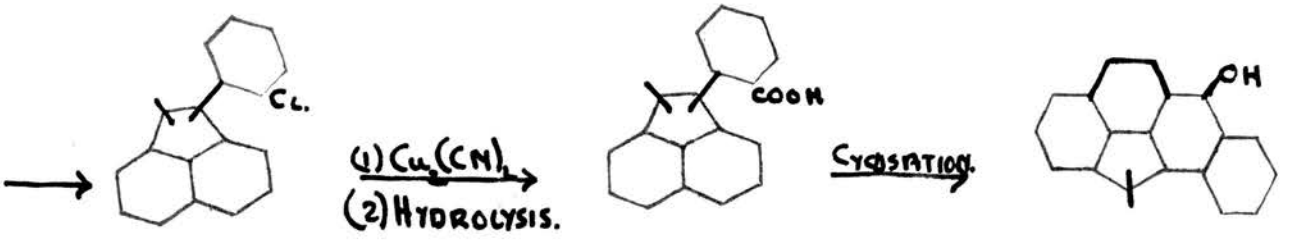


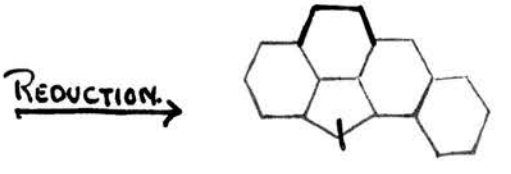


The structure of the 2:3-benzophenanthrindene was known by its synthesis (Fieser and Cason, J.A.C.S., 62, 432) Scheme 31.

SCHEME 31







That the succinoylation entered the 2-position was shown by dehydrogenating the dihydrophenanthryl-γ-butyric acid to give the corresponding phenanthryl-γ-butyric acid which on cyclisation gave a different benzophenanthrindene-4:5-methylenechrysene (page 68).

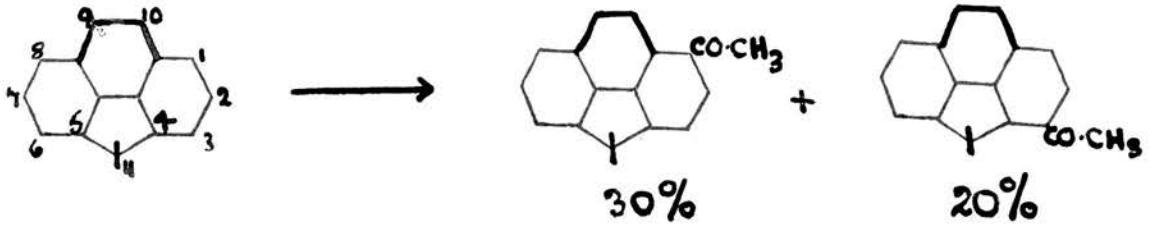
The Substitution Reactions of Acenaphthene

The substitution reactions of acenaphthene have been reviewed by Everest (loc.cit., page 1 et seq.). The essential features of its chemistry are the readiness with which the 3-position suffers substitution. Nitration and sulphonation however have both been shown to give some quantity of the 1-isomer as well. Disubstitution is more complex but dinitration has been shown to give the 3:4-isomer. Nitration of 3-acetamidoacenaphthene gives the 2-nitro derivative. The Skraup reaction of 3-aminoacenaphthene, as expected, gives cyclisation in the 2-position.

Acenaphthenequinone nitrates in the 3-position and dinitrates to give the 3:4-dinitro derivative; again it resembles acenaphthene except that the reactivity is reduced.

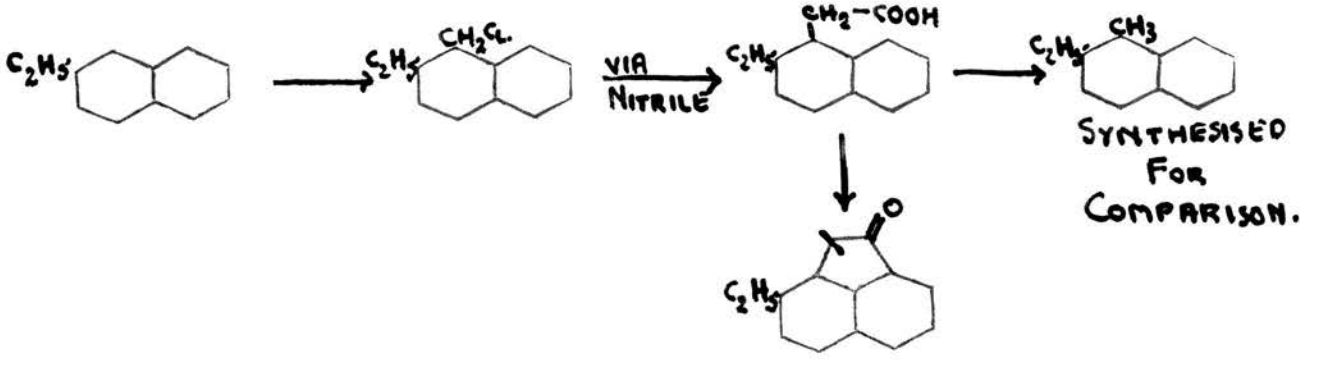
The Reactions of Phenanthrindene

(1) Monosubstitution. Bachmann, W.E. and Sheehan (J.A.C.S., 1941, 63, 2598) have shown that acetylation gives 30% of the 1-acetyl and 20% of the 3-acetyl compounds.



The structures were shown by reduction to the corresponding ethyl compounds which were synthesised.

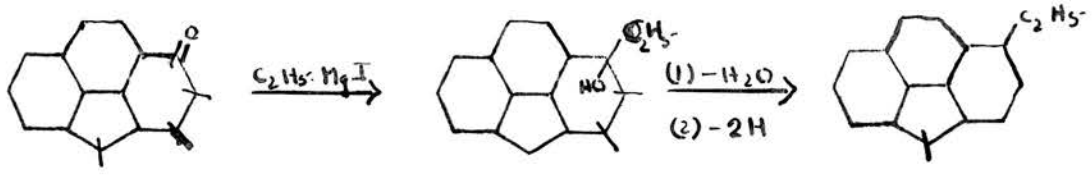
3-Ethylphenanthrindene.



The 1-ethyl-7-acenaphthenone was employed in the synthesis shown on page 9, to give 3-ethylphenanthrindene. The 1-ethyl derivative was prepared from the 1-keto-1:2:3:3a-tetrahydrophenanthrindene (page 9) by the Grignard reaction and

the subsequent reactions shown below (Scheme 32).

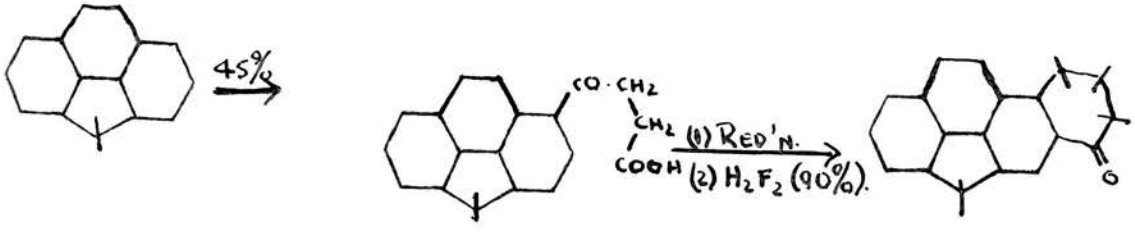
SCHEME 32



Disubstitution.

Fieser and Cason (J.A.C.S. 1940 62 1293-8) have succinoylated phenanthrindene and converted the product to 1,2-benzphenanthrindene by the scheme shown.

SCHEME 33

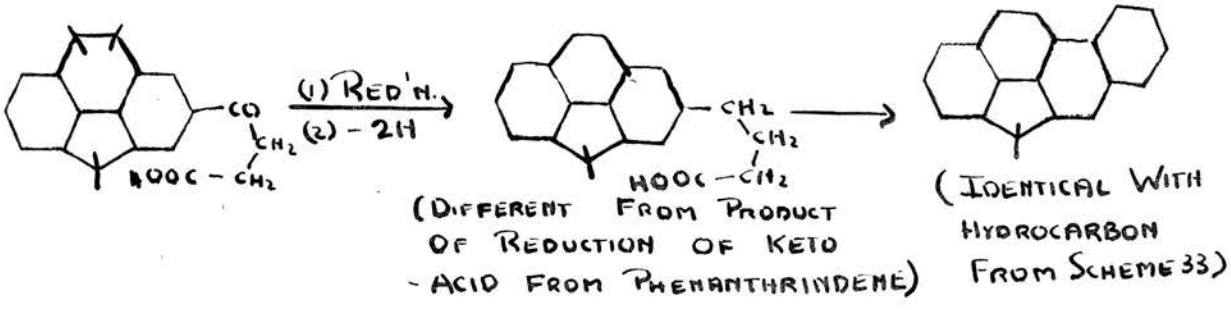


+ other keto acids not isolated

(1) Clemmensen
(2) DEHYDROGENATE

The structure of the hydrocarbon and the original succinoyl derivative was shown as follows (Scheme 34)

SCHEME 34



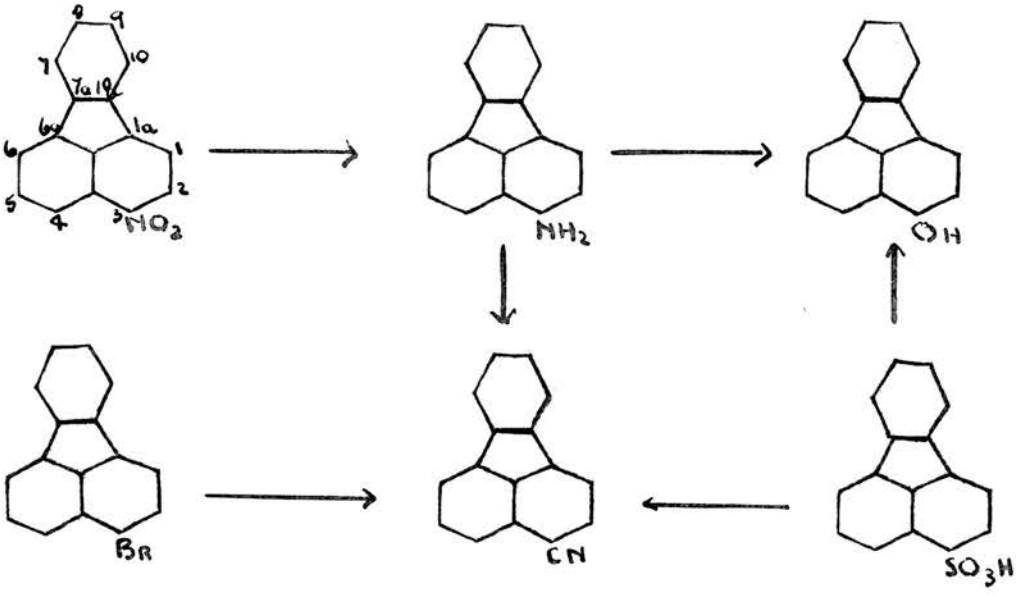
If the product above had been the 3-acid the hydrocarbon resulting would have been the 2,3-benzphenanthrindene but it was in fact 4,5-methylenechrysene.

Like fluorene the methylene group is reactive and Kruber (loc.cit.) isolated the hydrocarbon as its sodium salt. It condenses with benzaldehyde readily giving a benzylidene derivative.

Fluoranthene.

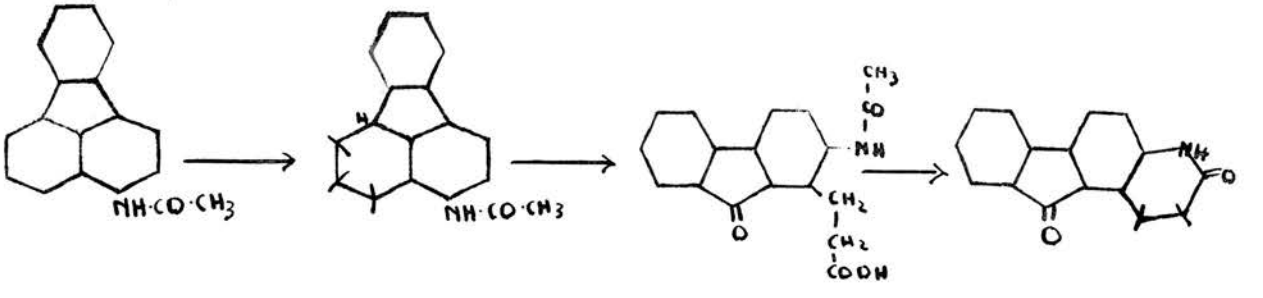
Fluoranthene has been shown to suffer monosubstitution in the 3-position, by the researches of von Braun and his school. The monobromo, mononitro and monosulphonic acids were inter-related by the classical procedures of Scheme 35.

SCHEME 35



The amino compound was then orientated (von Braun and Manz, Ber. 1930 63 2608) by the Scheme 36.

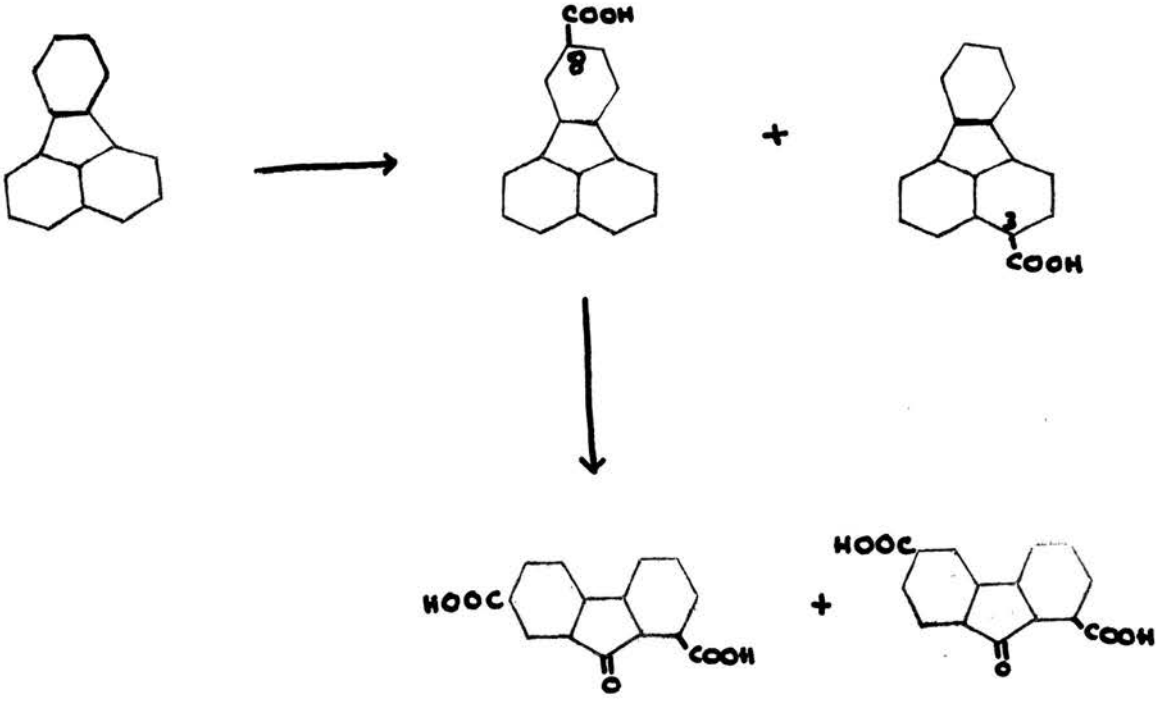
SCHEME 36



The isolation of the lactam demonstrates the position of the amino group relative to the point of fusion of the reduced ring.

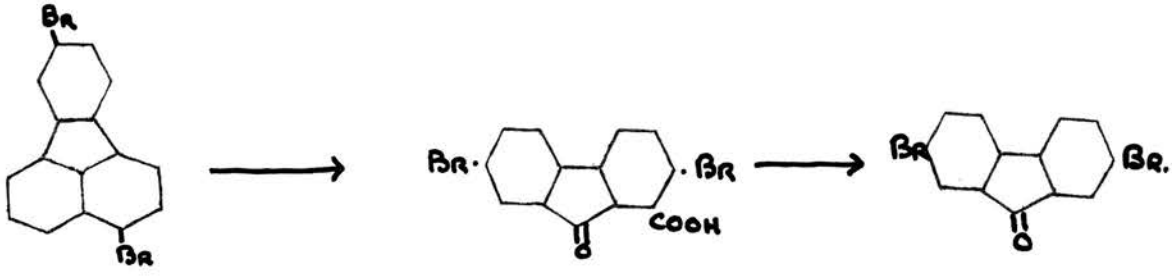
The Friedel Crafts carboxylation yielded two products one of which, present in smaller yield was identified by von Braun and Manz as the 3-acid (Ann., 1932,496,107) by conversion to 3-aminofluoranthene. The other acid was shown to yield on oxidation two acids, one of which was the known 1:7-fluorenone dicarboxylic acid. This reduced the possiblities and permitted the identification of the product as the 8-acid (Scheme 37)

SCHEME 37



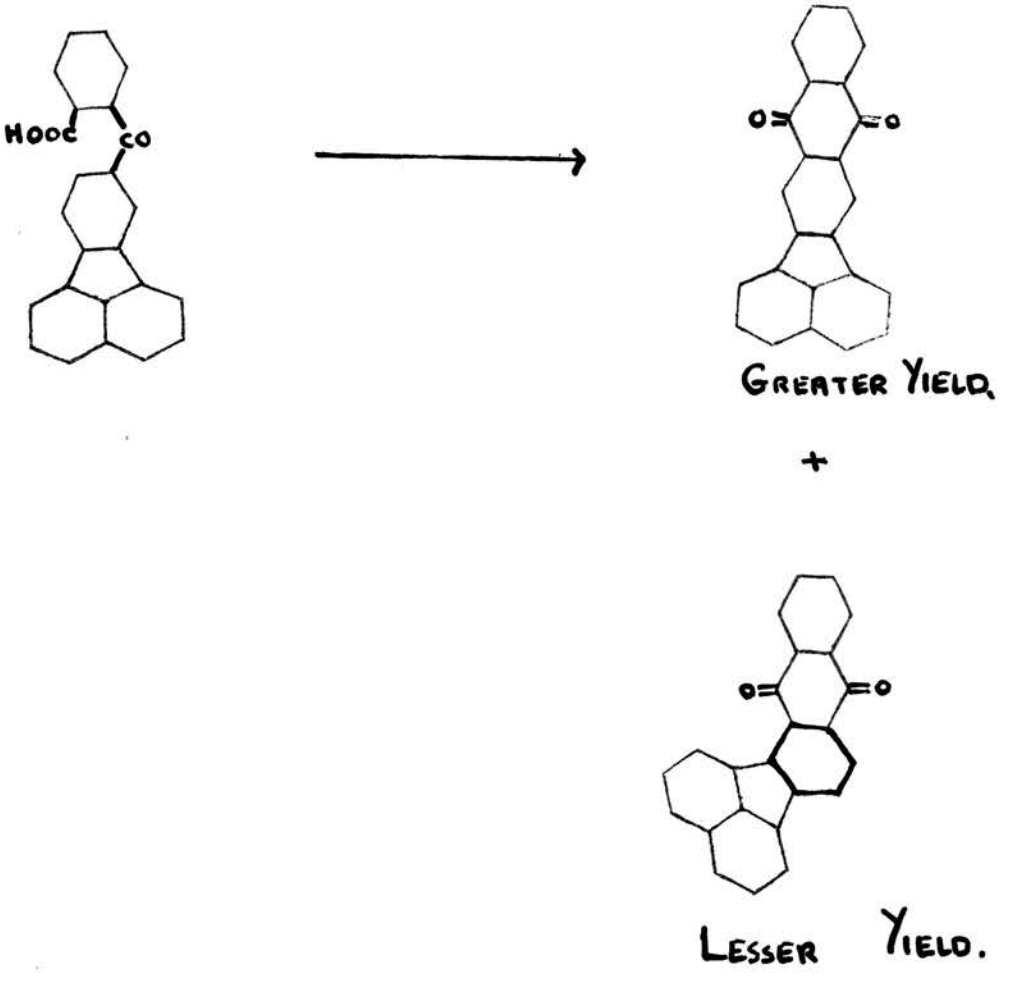
Disubstitution in the fluoranthene series has been examined by Campbell and Easton, and Campbell, Rayment, Easton and Wiltshire. The final conclusions will be discussed in a forthcoming paper by the latter workers (private communication). It has been shown that positions 3 and 8 (or perhaps in certain cases 9) are involved in the disubstitution. Rayment (Ph.D. Thesis, Edinburgh, 1949) oriented 3:8-dibromofluoranthene by oxidation to 2:7-dibromofluorenone-1-carboxylic acid which decarboxylated to give 2:7-dibromofluorenone (Scheme 38).

SCHEME 38



Cyclisation of 8-(o-carboxybenzoyl)-fluoranthene has been shown to give two isomeric 7:8-acenaphthenylanthraquinones but the isomer derived from cyclisation in the 9-position predominated over the isomer from cyclisation in the 7-position (Campbell, Reid and Marks forthcoming paper; private communication).

SCHEME 39

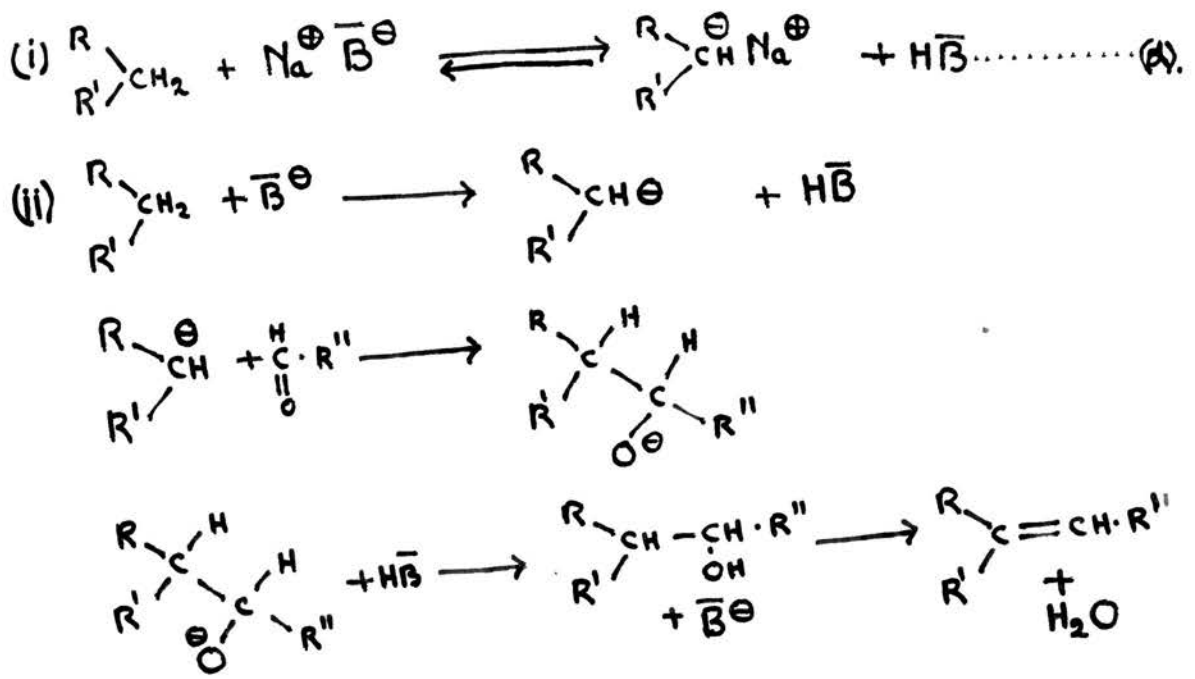


DISCUSSION

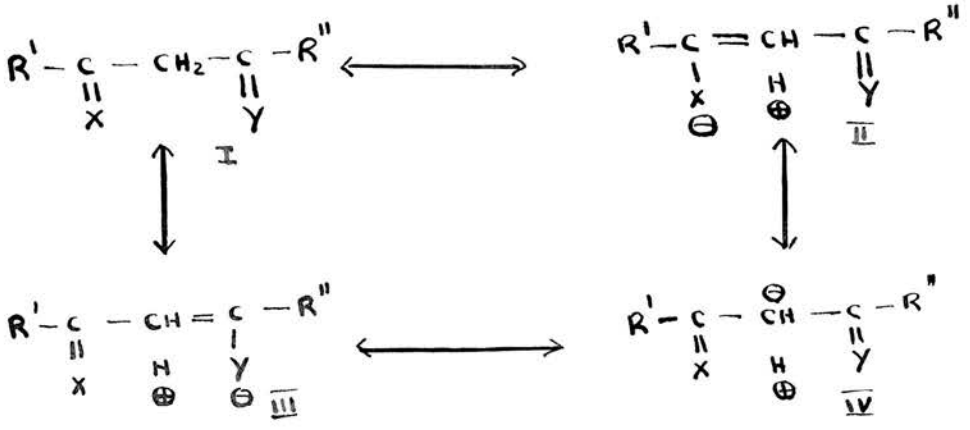
(i)

The Active Methylene Group in Indene Fluorene and Phenanthrindene

Indene, fluorene and phenanthrindene all give derivatives with alkali metals and strongly basic derivatives of these metals; they also suffer condensation reactions in presence of basic catalysts. This reactivity must exist by virtue of the "acidity" of the methylene group. The reactivity of the methylene group may be exemplified in general terms by the two series of equations given below:



This "acidity" is due to the tendency for unsaturated groups to withdraw electrons from a methylene group (cf. enolisation).



If the molecule is in its normal state, the structure I is most stable and contributes to the resonance to a high degree whereas II, III and IV are of minor importance. When a base is added, an equilibrium is created (e.g. see equation (i)) between neutral molecules and ions and this equilibrium is dependent on

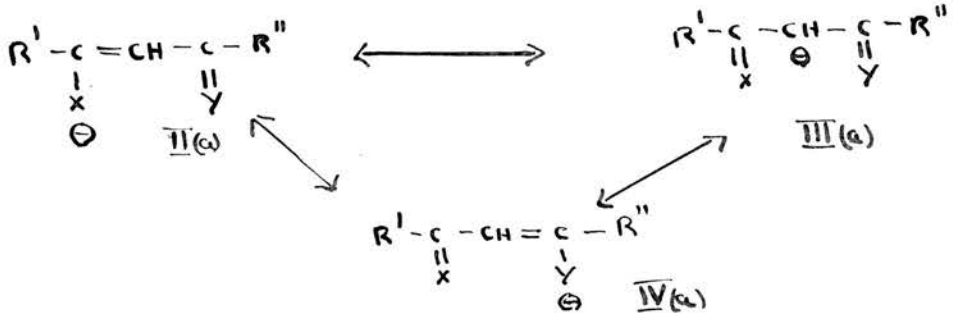
(1) the effectiveness of the base (i.e. its basic strength)

(2) the conditions (i.e. concentration, temperature, nature of solvent etc.)

(3) the inherent stability of the ionic type.

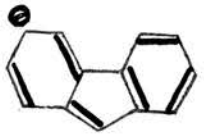
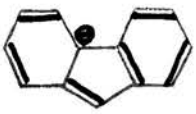
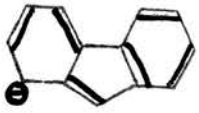
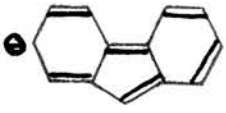
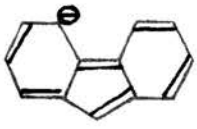
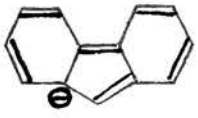
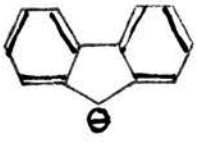
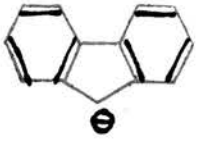
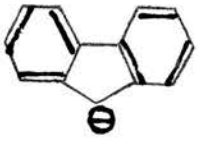
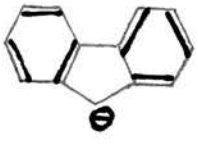
This latter factor is controlled by the relative contributions of the 3 canonical structures II(a), III(a) and

IV(a), to the final resonance hybrid.

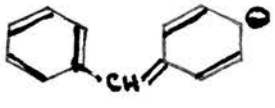
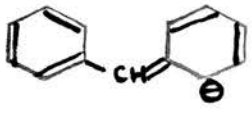
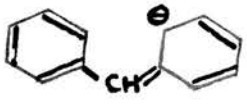
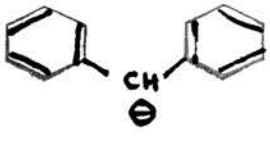
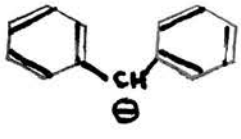


Under the most favourable conditions these will contribute equally and the ion will be stable and under the least favourable conditions, when III(a) solely represents the structure, the charge localisation and the absence of resonance stabilisation will reduce the stability of the ion to a significant degree.

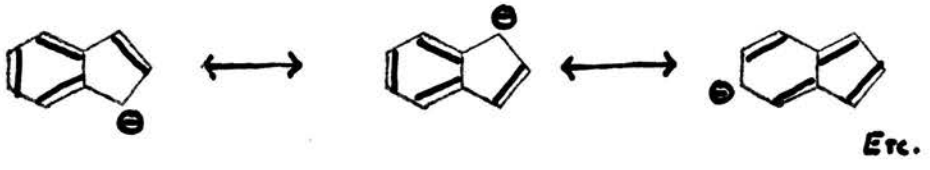
The relative stability of the ions and the essential reactivity of the methylene group must be dependent on the groups $R'-\underset{\underset{X}{\|}}{C}-$ and $R''-\underset{\underset{Y}{\|}}{C}-$. The difference between fluorene, which readily gives a sodio-derivative, and diphenylmethane, which is much less reactive, must be interpreted on a basis of the difference between $R'-\underset{\underset{X}{\|}}{C}-$ and $R''-\underset{\underset{Y}{\|}}{C}-$ for the two compounds. A few of the contributing structures of the fluorene ion are shown below (restricted to one ring).

It is obvious that there is a greater number of contributing ionic structures for fluorene than for diphenylmethane for which the structure, corresponding to those given for fluorene, are given below.

Similarly the ion derived from indene can be represented as the hybrid of several structures of which the following are typical

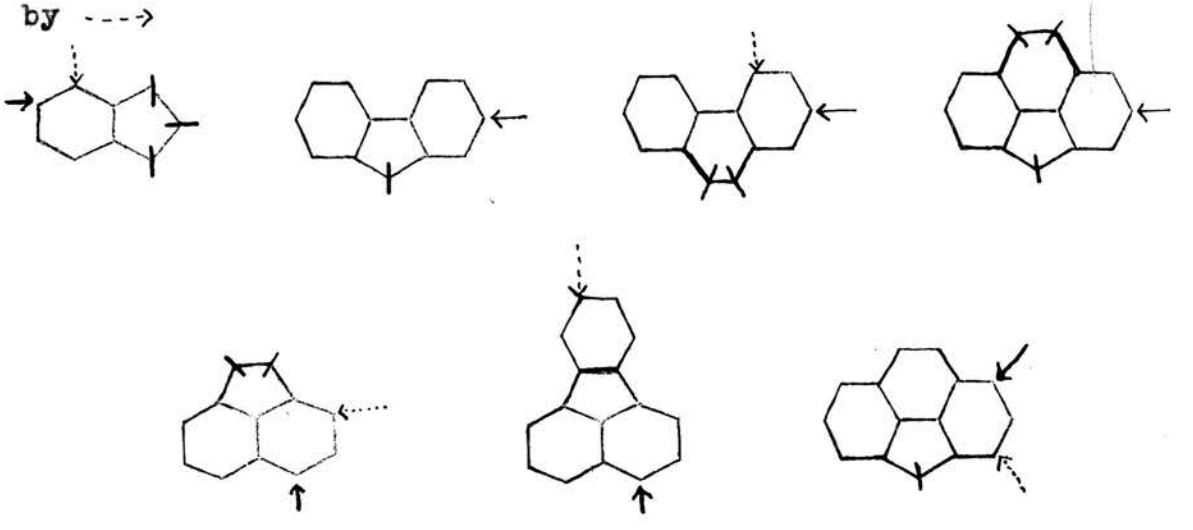


It is obvious that the 2:3-double bond of the uncharged molecule will lose its identity when ionisation occurs. This is the obvious explanation of the difficulty often experienced in the indene series, namely, that syntheses calculated to give say a 5-substituted indene often give a mixture containing the 6-substituted derivative as well.

(ii)

Monosubstitution

In the diagram below the principal sites of substitution are indicated by ⟶ and the secondary sites by ⇢



Hydrindene resembles o-xylene in that monosubstitution occurs para to one of the alkyl groups (in o-xylene methyl in hydrindene, $\rangle CH_2$, methylene). Fluorene, dihydrophenanthrene and dihydrophenanthrindene are similar to biphenyl, the 2-position (corresponding to 4 in biphenyl) being particularly reactive. In dihydrophenanthrene the 4-position (corresponding to 2 in biphenyl) suffers attack to a small extent. Preliminary examination of the reactions of these compounds indicates that, as far as monosubstitution is concerned, there is no obvious difference

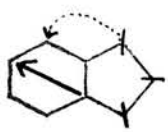
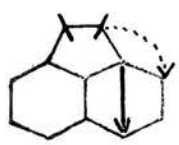
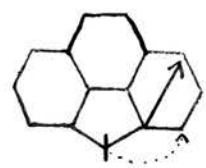
in the nature of the reactions, thus showing that the five-membered ring does not affect the fundamental reactivity of the biphenyl type.

In acenaphthene the 3-position is preferred but the 1-position is also susceptible to substitution. Phenanthrindene resembles acenaphthene and phenanthrene in structure; in reactivity the resemblance to acenaphthene is patent. Phenanthrindene substitutes principally in the 1-position i.e. para to the methylene group which corresponds to the reactive 3-position of acenaphthene. The phenanthrene type of substitution, which would involve substitution principally in the 3-position, is sublimated to a considerable extent in phenanthrindene. The monosubstitution reactions of phenanthrindene may be regarded as evidence of the strong directing influence of the 11-methylene group to the "para" position; the reactivity of the 3-position may be regarded as the resultant of the "ortho" influence of the methylene group and the normal phenanthrene reactivity.

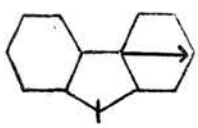
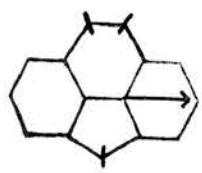
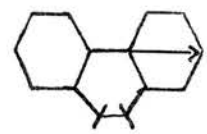
Fluoranthene resembles acenaphthene in the reactivity of the 3-position. This, however, also corresponds to the reactive 2-position of fluorene; the reactivity of the 8-position in fluoranthene is also in accord with the fluorene analogy as it also corresponds to a 2-position in fluorene.

In monosubstitution it is apparent that the pattern of the reactivity is not sensibly influenced by the absence or presence of a five-membered ring but rather by the directing influence of an alkyl group or the phenyl group.

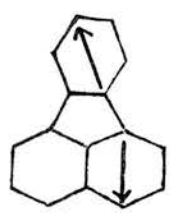
Directing Influence of Alkyl Group

Directing Influence of Phenyl Group

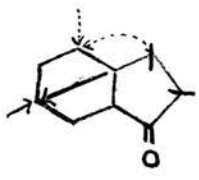
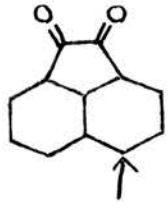
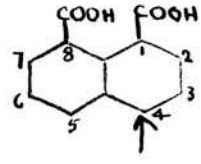
Fluoranthene apparently fits into the last category as it may be considered as a 1-phenyl naphthalene - an analogy fully discussed by von Braun

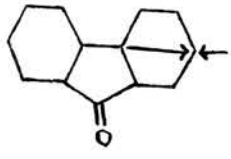
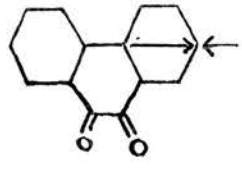


This approach to the question is obviously an over-simplification as the importance of "fine structure" is important. (See, however, Section IV.)

The monosubstitution reaction of ketonic derivatives is of interest for it follows an almost identical path, Scheme 40)

SCHEME 40

In these cases the nature of the reaction is the same, but conditions necessary to procure reaction are harsher.

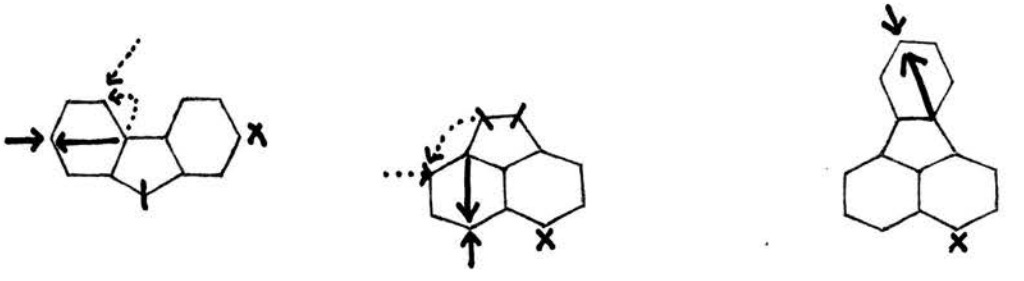
For 1-hydrindone, fluorenone and phenanthraquinone the directing influence is obviously the same as for the hydrocarbons; however, in the case of acenaphthenequinone there is no obvious directing influence favouring 3 substitution. Acenaphthenequinone resembles naphthalic acid in its monosubstitution reactions in so far as the 4-position of 1:8-naphthalic acid is principally reactive. The effect of the carbonyl groups in both cases is to reduce the normal reactivity of the naphthalene nucleus.

There is no apparent evidence that the 5-membered ring in acenaphthenequinone confers any special reactivity on any position in the ring system.

Disubstitution

(α)

When the primary substituent is not strongly ortho-directing substitution follows the pattern shown below - X representing the primary substituent and ⟶ and ⋯⋯> the main and secondary reactive positions respectively.

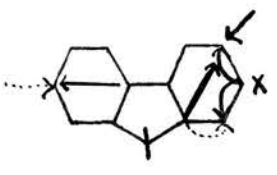


In fluorene the reactivity is typical of the biphenyl structure, position 7 being predominantly attacked, but position 5 (cf. dihydrophenanthrene monosubstitution) also undergoing substitution. In 3-substituted acenaphthenes the other peri-position (4) is most readily attacked but one of the ortho positions, to the ethylene bridge can also be involved. In fluoranthene the positions corresponding to 2 and 7 in fluorene are the principal sites of disubstitution. The peri-position,4,is not attacked

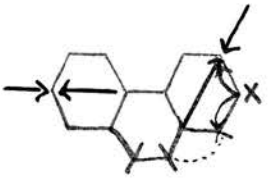
in dibromination possibly because of the steric effect of the bromine atom at 3.

(β)

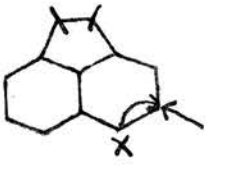
When the primary substituent directs to the ortho position then the principal positions of substitution are shown below.



X = NH·Ac
OR. NH·Ts



X = OH



X = NH·Ac

In the case of fluorene and dihydrophenanthrene the factors involved are

(1) the para directing influence of the phenyl group (Strong).

(2) the ortho directing influence of the substituent X (Strong).

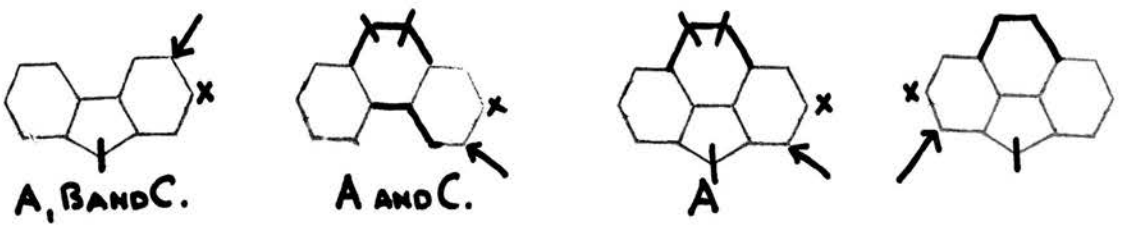
(3) the para directing influence of the alkyl group (Strong).

(4) the ortho directing influence of the alkyl group (Weak).

The 7-position and the 3-position together are favoured in both cases. A mixture of products containing a considerable proportion of each constituent (7-and 3-substituted-2-X-compounds) is obtained. The decisive factor favouring position (3) rather than (1) in both cases, is the strong directing influence of the alkyl group to the para-position (3), relative to the weaker influence of the alkyl group to the para-position (1). For acenaphthene the only ortho position available is the 2-position.

(ϰ)

When due to the nature of the primary substituent a cyclisation must occur in the ortho position the following formulae represent the essential facts:



A ≡ Cyclisation of 2: ϰ -butyric acid

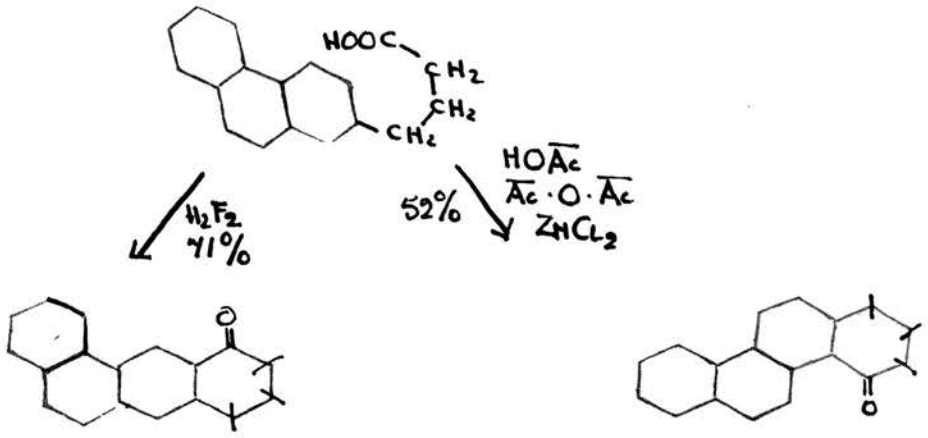
B ≡ Cyclisation of 2, — (o-carboxyphenyl)-methylfluorene

C ≡ Skraup syntheses.

Fluorene and dihydrophenanthrene are very similar in that the 3-position is favoured for the cyclisation of suitable 2-substituted derivatives. Dihydrophenanthrindene presents an interesting contrast for the cyclisation of any 2-substituted derivative, if it occurs unidirectionally, and will give the result of the competitive directing of the ethylene group and the methylene group - and it is evident that the ethylene group succeeds, for cyclisation occurs preferentially in the 3-position which is para to the ethylene group.

The cyclisation of indeno-phenanthrene-2:γ -butyric acid is of interest because it occurs in the 3-position rather than the 1-position - which from the monosubstitution would be expected to be more reactive. Before judgment is passed on this it should be recalled that the Skraup synthesis of 2-aminophenanthrene occurs in the 1-position whereas the cyclisation of the 2:γ -butyric acid of phenanthrene may occur in either the 1 or the 3-position, depending on the cyclisation agent employed, Scheme 41.

SCHEME 41



The specificity of this method (i.e. cyclisation of the γ-δ-butyric acid) of estimating relative reactivity of ortho positions must be questioned but it should be remembered that hydrogen fluoride which gave the unexpected result for phenanthrindene also gave the anomalous result for phenanthrene. Until further work is done - Skraup reaction etc. - no judgment may legitimately be passed.

Polysubstitution falls again into a pattern allied to that for monosubstitution. In the cases of fluorene dihydrophenanthrene and dihydrophenanthrindene, the biphenyl type reactivity is operative. In acenaphthene and phenanthrindene the directing influence of the alkyl group is impressed on the inherent reactivity of the naphthalene and phenanthrene nuclei.

SECTION III

THE SYNTHESIS OF FLUORENE AND ITS DERIVATIVES

INTRODUCTION

The synthetic methods employed to synthesise fluorene and its derivatives are considered under the following headings:

(i) Syntheses from other fluorene derivatives.

(ii) Syntheses from biphenyl derivatives.

(iii) Syntheses from benzophenone or diphenylmethane derivatives.

(iv) Syntheses from phenanthraquinones.

(v) Syntheses from hydrindene and its derivatives.

(i)

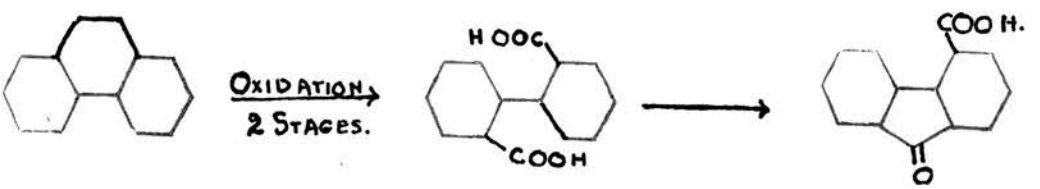
Syntheses from other fluorene derivatives

The substitution reactions of fluorene have been adequately discussed in Section II and the simple 2-substituted and 2:7-disubstituted fluorene derivatives may be obtained either directly or indirectly from the substitution products. Two fluorene compounds — fluorenone-1-carboxylic acid and fluorenone-4-carboxylic acid — can be obtained from fluoranthene and phenanthrene (Schemes 42 and 43) respectively

by simple processes which make them suitable intermediates for the preparation of 1-and 4-substituted fluorene derivatives.

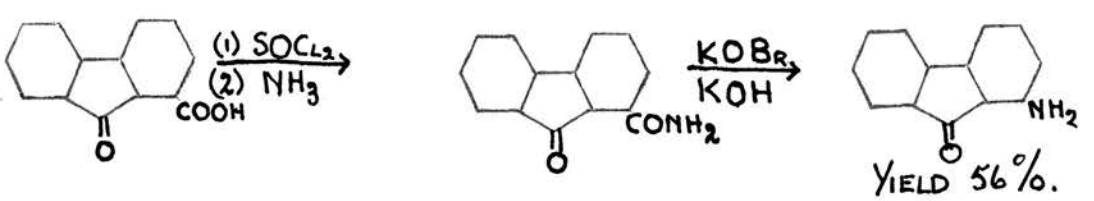
SCHEME 42

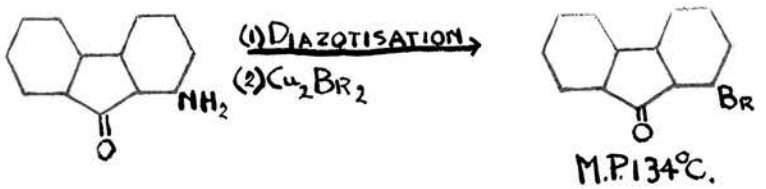
SCHEME 43



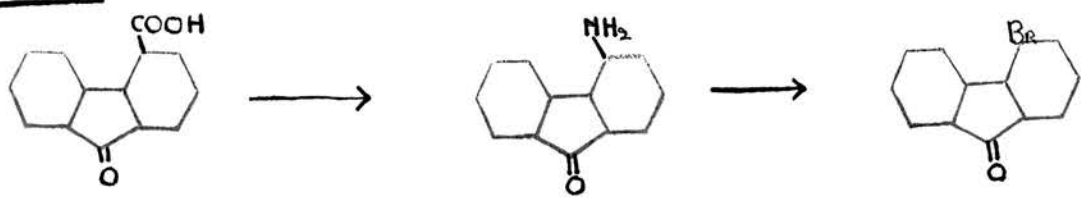
As examples of the use of these acids in synthetic work, the preparations of 1-and 4-bromofluorenones may be cited, Scheme 44, (Huntress, Pfister and Pfister, J.A.C.S., 1942, 64, 2845-9; cf. Goldschmiedt, Monatsh., 1902, 23, 893-5).

SCHEME 44



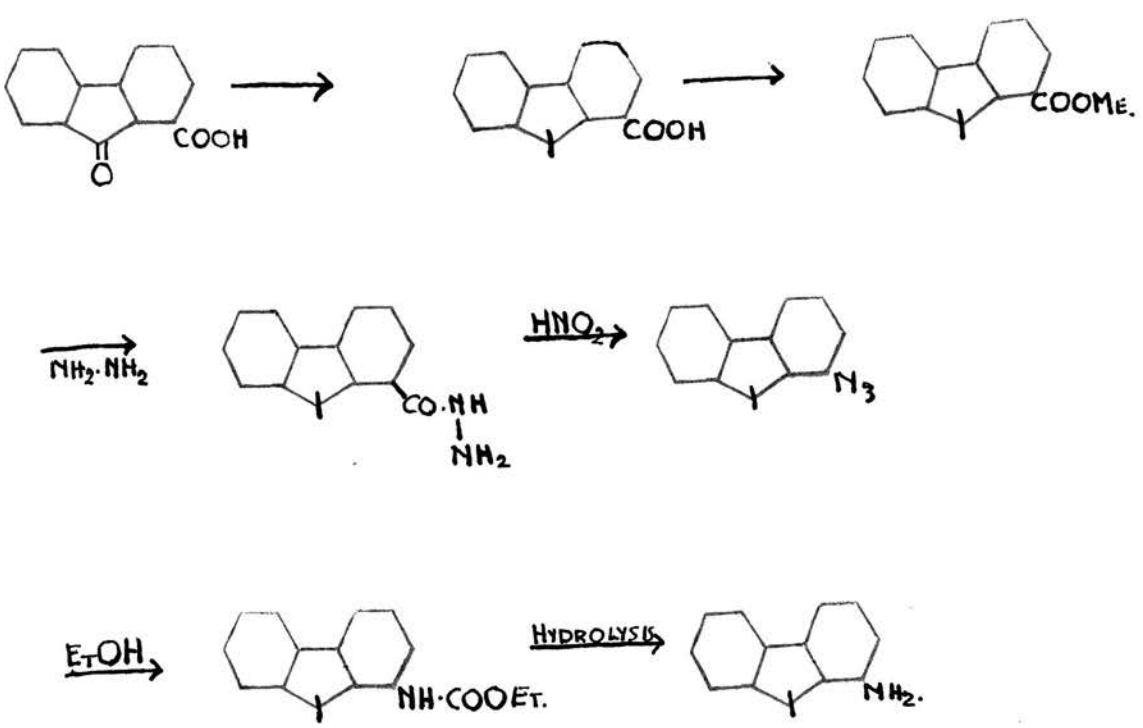


Similarly



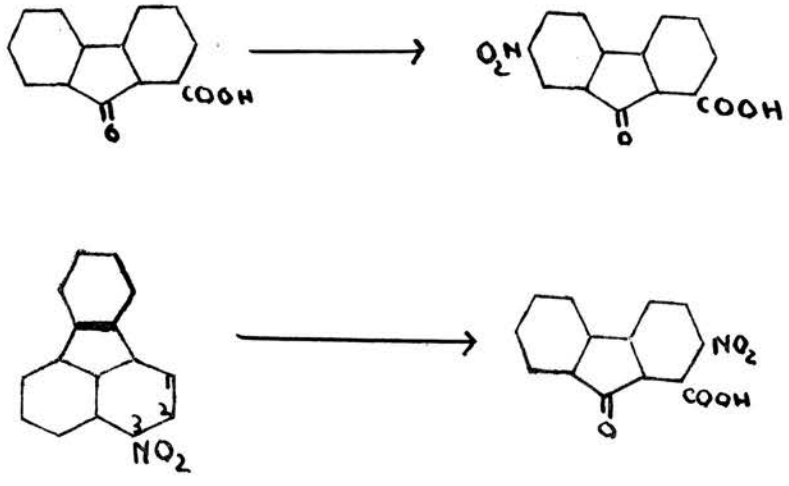
Bergmann and Orchin (J.A.C.S., 1949, 71, 1111-2) have synthesised 1-aminofluorene from fluorene-1-carboxylic acid derived from fluorenone-1-carboxylic acid, Scheme 45.

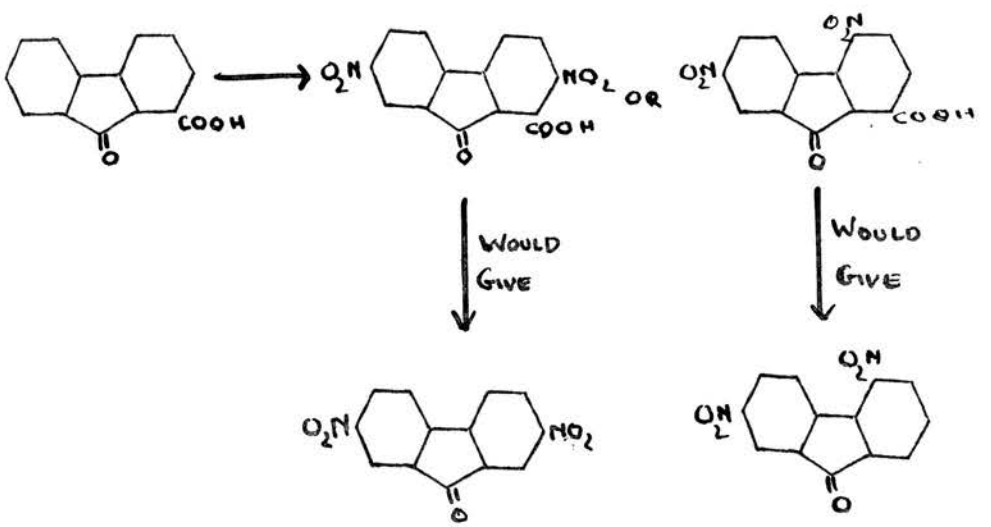
SCHEME 45



Nitration of fluorenone-1-carboxylic acid (Fittig and Liepmann, Ann., 1880, 200, 8) gives a mono-nitro fluorenone-1-carboxylic acid(M.P. 245 - 6°C) 2-nitrofluorenone-1-carboxylic acid (M.P. 233- 5°C.) was subsequently isolated from the oxidation of 3-nitrofluoranthene (von Braun, Manz and Kratz, Ann., 496, 170-96). It is highly likely that the Fittig and Liepmann acid is the 7-nitrofluorenone-1-carboxylic acid. A dinitrofluorenone-1-carboxylic acid (page 273) has been prepared, but only on a small scale, by direct nitration; it is likely to be either the 2:7-dinitrofluorenone-1-carboxylic acid or the 4:7-dinitrofluorenone-1-carboxylic acid. This point could be proved by further nitration of the von Braun, Manz and Kratz acid and comparison of the products or by decarboxylation and comparison with 2:7-dinitrofluorenone and 2:5-dinitrofluorenone (Scheme 46).

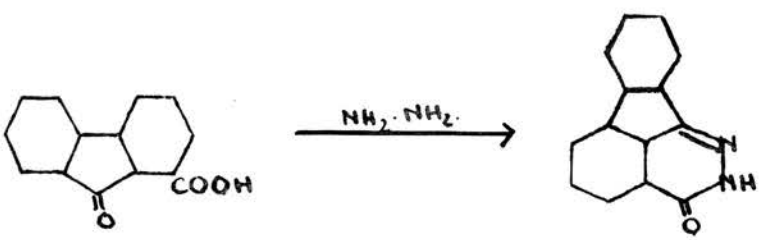
SCHEME 46





Fluorenone-1-carboxylic acid has been shown to react with hydrazine hydrate to give 3-keto 2:3-dihydro-1:2-diaza-fluoranthene (Scheme 47).

SCHEME 47



This derivative was obtained in good yield and should prove useful for identifying and characterising fluorenone-1-carboxylic acids. It should also be pointed out that this compound is fairly stable to alkali and it is likely, therefore, that it will interfere with the Wolff-Kishner reduction of the keto group, except under sufficiently critical conditions which would cause decomposition of the hydrazone as quickly as it was formed before cyclisation to the hydrazide occurred.

(ii)

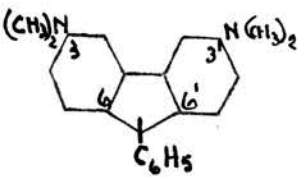
Syntheses from Biphenyl and its derivatives.

Although Adam (Compt. rend., 1886, 103, 207) has shown that methylene dichloride reacts with biphenyl to give fluorene under Friedel-Crafts conditions it is at once patent that this method is capable of little application in the syntheses of fluorene derivatives. The method is founded on the reactivity of the 2-position in the biphenyl structure, a reactivity which is much less than that of the 4-position. Methylene chloride is, further, bifunctional in the Friedel-Crafts reaction and when it reacts with a compound such as biphenyl which has at least two highly reactive positions the formation of a high percentage of polymers of the type shown must be expected.

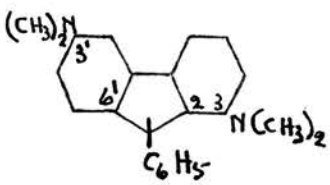
$$C_6H_5 \cdot C_6H_4 \cdot (CH_2 \cdot C_6H_4 \cdot C_6H_4)_x \cdot CH_2 \cdot C_6H_4 \cdot C_6H_5 \cdot$$

Only when the 2-position is especially favoured by suitable substitution can this reaction be expected to succeed in any degree. Dutt (J., 1926, 1171) by reacting 3:3'-di-(dimethylamino)-biphenyl with benzal chloride used the para-activating effect of the dimethylamino group to favour the 6-and 6'-positions. The 2-and 2'-positions ortho to

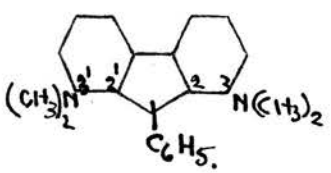
the dimethylamino groups must be expected to share some of the reactivity and the compounds B and C must reasonably be expected to be present with the compound A isolated by Dutt. The dimethylamino groups would also activate the 4- and 4'-positions, which are normally very reactive in biphenyl, in some degree, so again a polymer of the type shown above would probably be formed. In view of this it is not surprising that no yield of A is quoted by Dutt and that he reports difficulty in purifying by crystallisation.



A



B

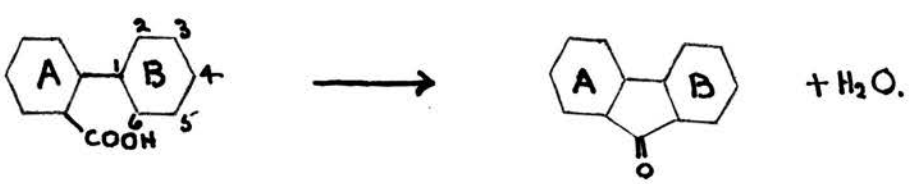


C

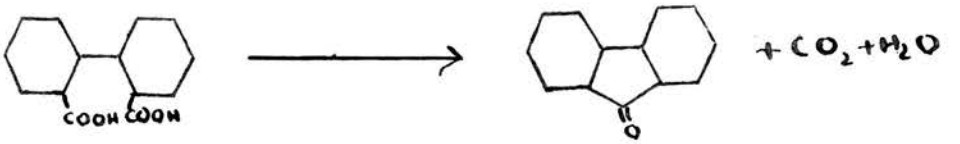
(Numbering refers to biphenyl)

Two specially useful methods are used to convert biphenyl derivatives into fluorene derivatives.

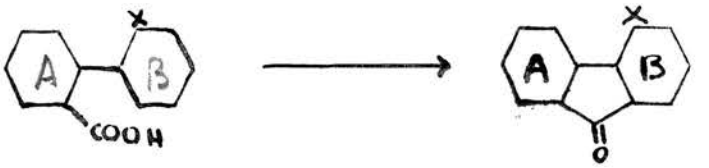
(a) the cyclisation of biphenyl-2-carboxylic acid and its derivatives



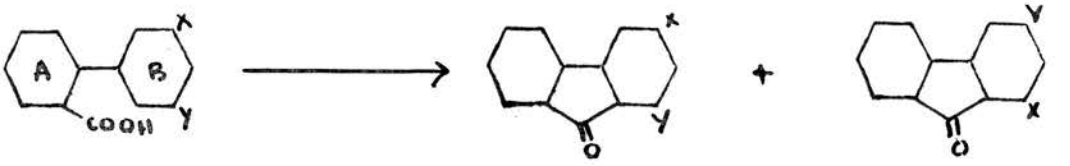
(β) the cyclisation of diphenic acid and its derivatives



The method by which fluorenones are prepared from substituted biphenyl-2-carboxylic acids has certain limitations. Substituents in ring A do not affect the cyclisation whereas a substituent in position 2 in ring B will direct cyclisation to the 6-position and vice versa. Stable groups in both the 2- or 6-positions will completely inhibit cyclisation.



A single substituent in positions 3 or 5 of ring B or two different substituents in positions 3 and 5 of ring B will in general lead to the production of two fluorenones.

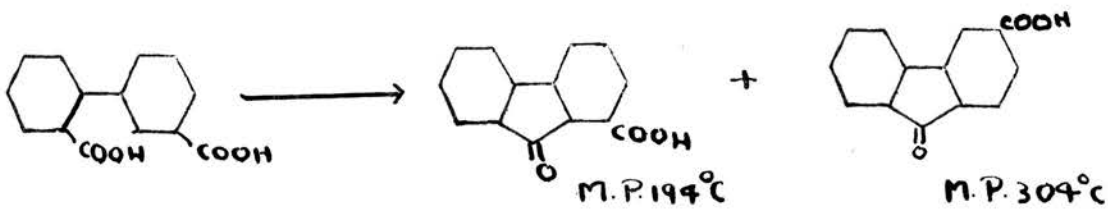


Position 4 by virtue of its symmetry does not affect the structure of the cyclisation product.

The effect of a substituent in position 2 of ring B is exemplified by the dehydrative cyclisation of diphenic acid which can only give fluorenone-4-carboxylic acid. A substituent in position 3 (Ring B) means that the determination of the position of the substituent in the two resulting fluorenones can only be made if at least one of the products can be identified. An example of this problem - a problem of importance in the later part of this thesis - is outlined below.

The isodiphenic acid, biphenyl-2:3'-dicarboxylic acid, can be obtained from fluorenone-1-carboxylic acid by alkaline fusion (Fittig and Liepmann, loc.cit., cf. page 249.). Mayer and Freitag (Ber., 1921, 54, 347) synthesised this acid by oxidation of the corresponding dimethylbiphenyl and cyclised it to obtain fluorenone-1-carboxylic acid in 12% yield. This cannot be accepted as conclusive evidence of the structure of the 1-acid as the 3-acid may simultaneously be formed. Indeed, on repeating the cyclisation of the acid (page 250), fluorenone-3-carboxylic acid was also isolated — albeit with difficulty. The conslusive synthesis of fluorenone-1-carboxylic acid by Sieglitz (page 251) when coupled with the disparity between the melting points of fluorenone-1-carboxylic acid and fluorenone-3-carboxylic acid (194°C. and 304°C).

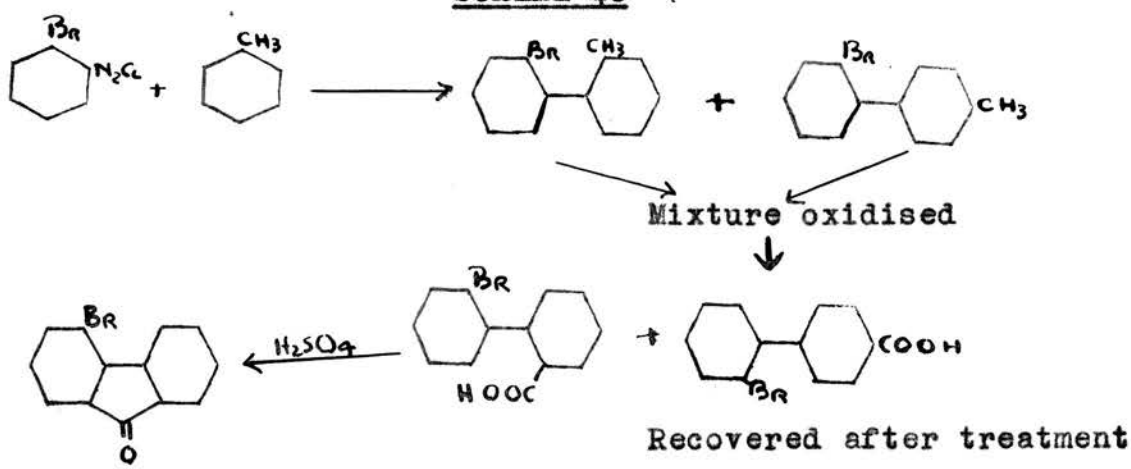
respectively) permitted the confident assignment of the structures to the two isomers isolated.



The cyclisation procedures vary but little from acid to acid but the number of methods used to obtain the requisite biphenyl-2-carboxylic acids is large. A few examples are described below.

(i) Heilbron, Hey and France (J., 1938, 1369) prepared 4-bromofluorenone by the method indicated in Scheme 48.

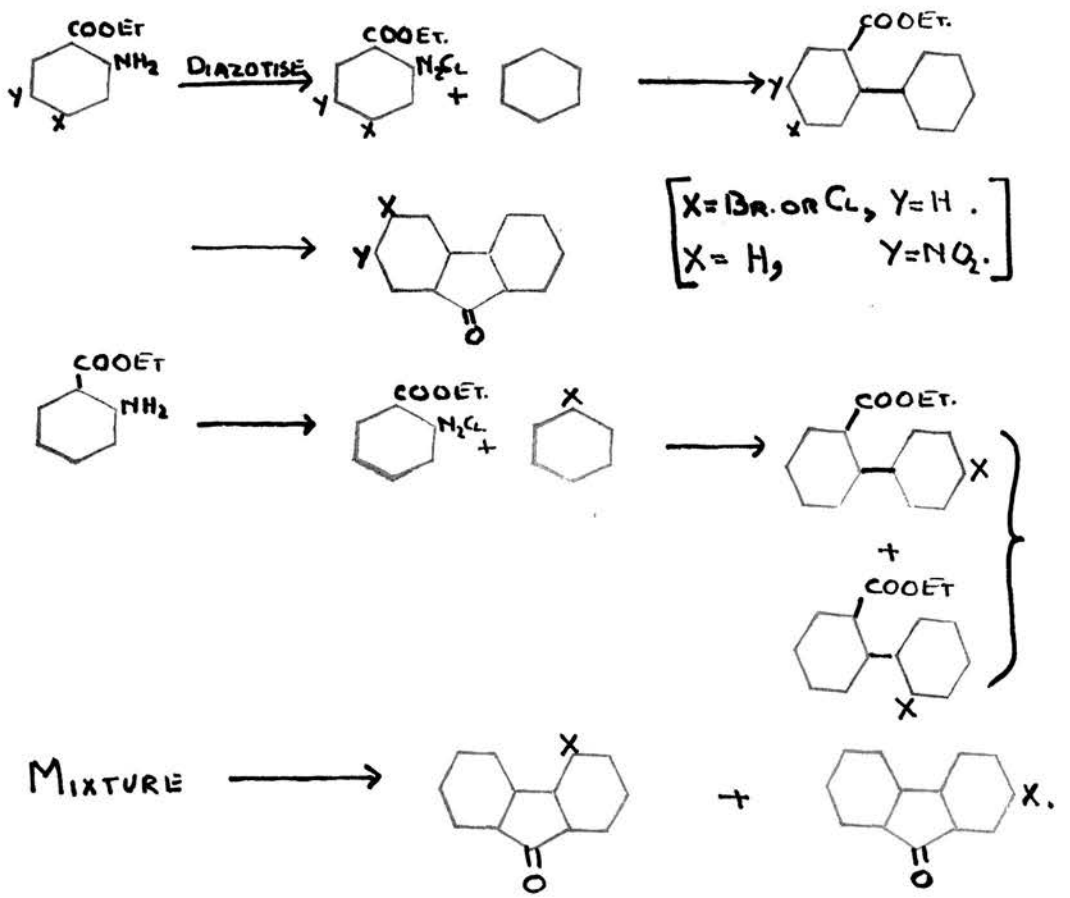
SCHEME 48



The 2-bromobiphenyl-4'-carboxylic acid was stable to sulphuric acid under the conditions employed to cyclise the isomeric acid.

(ii) Heilbron, Hey and Wilkinson (J., 1938, 113) obtained substituted biphenyl-2-carboxylic acids from suitable derivatives of anthranilic acid by the procedure of Scheme 49.

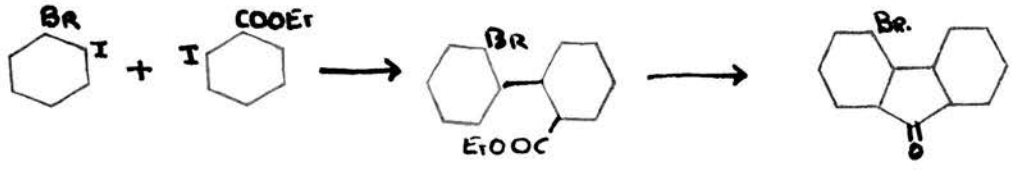
SCHEME 49



In the latter case the resulting mixture of 2 and 4 halogeno fluorenones was found to be difficult to separate.

(iii) Miller and Bachman (J.A.C.S., 1935, 57, 2445) claim to have synthesised 4-bromofluorenone from 2-bromobiphenyl-2'-carboxylic acid by the route shown in Scheme 50.

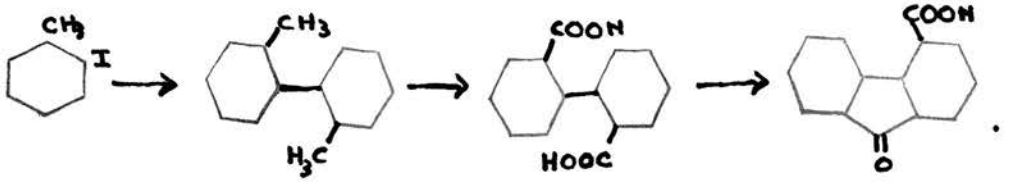
SCHEME 50



The product differs in physical properties from that of Heilbron, Hey and France, and Huntress, Pfister and Pfister (see pages 96, 109). Huntress, Pfister and Pfister (loc.cit.) could not repeat this unequivocal synthesis and showed that an alternative reaction sequence (page 109), which Miller and Bachman claim to give a product identical with that from the above, in fact gave 1-bromofluorenone.

(iv) Diphenic acid and hence fluorenone-4-carboxylic acid may be considered as being derived from ortho iodotoluene by the reaction sequence of Scheme 51.

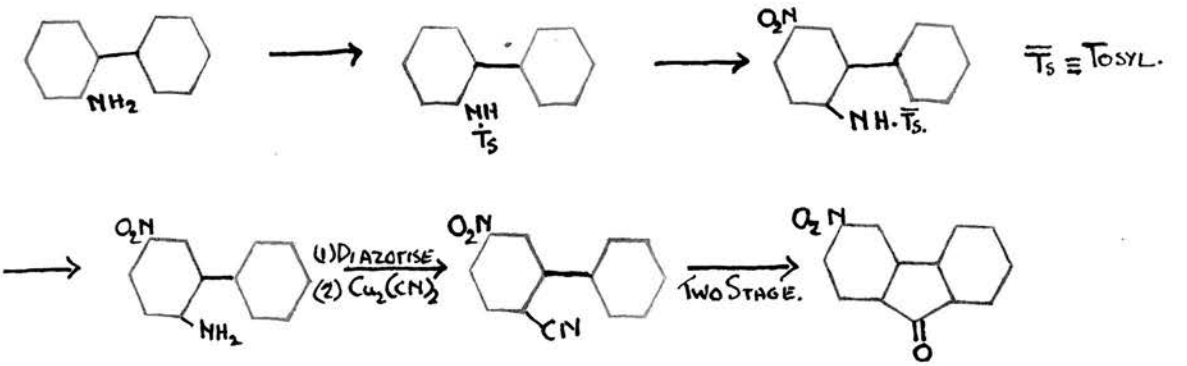
SCHEME 51



(Ullmann and Meyer, Ann., 332, 42; Jacobson, Fabian, Ber., 28, 2555.)

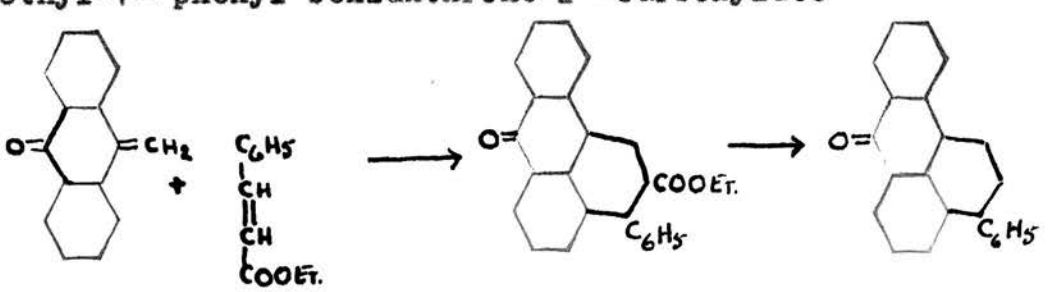
(v) The synthesis of 3-nitro-fluorenone by Ray and Barrick (J.A.C.S., 1948, 70, 1492) who used 2-aminobiphenyl as starting material is shown in Scheme 52.

SCHEME 52



(vi) Biphenyl-2-carboxylic acid derivatives have also been obtained by diene syntheses with cinnamic acid.

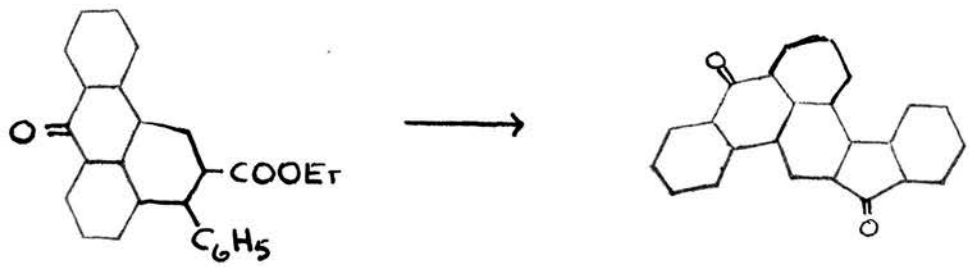
(a) Swain and Todd (J., 1942, 626) condensed 9-methylene anthrone with ethyl cinnamate in nitrobenzene and obtained ethyl-1'-phenyl benzanthrone-2'-carboxylate



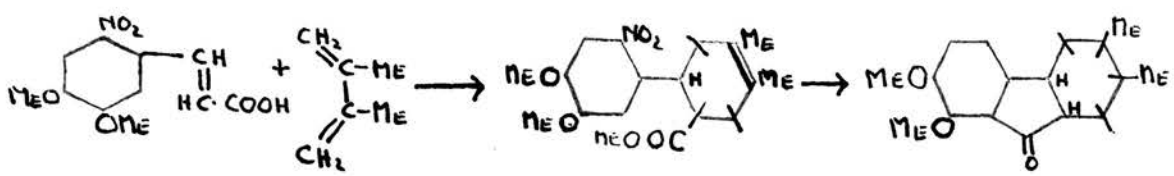
[+ 4H to nitrobenzene]

The product was decarboxylated giving 1-phenyl mesobenzanthrone; cyclisation gave 1"-keto-indeno-2"; 3"; 2'; 1'

benzanthrone.



(β) The synthesis of 1:2:3:4:4a:1a-hexahydra-9-fluorenones has been obtained by the cyclisation of the hexahydrobiphenyl-2-carboxylic acids obtained in turn by hydrogenation of the products of diene addition of cinnamic acid derivatives and suitable dienes, e.g.



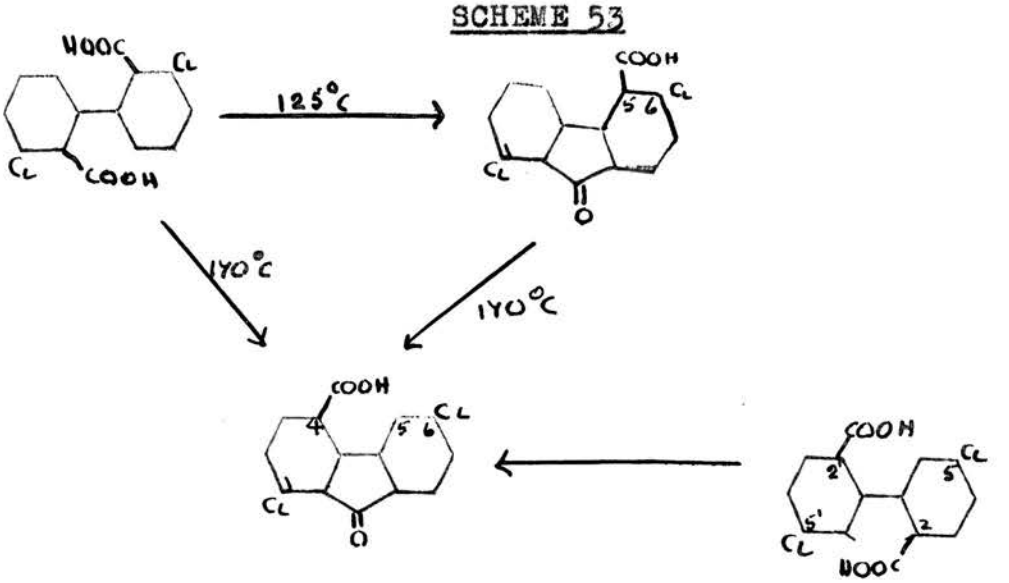
(Adams, McPhee, Carlin and Wicks, J.A.C.S., 1943, 65, 356; cf. Tujise, Horiucki and Takahashi, Ber., 1936, 69, 2102; Sugasawa, Kodama and Hara, Chem. Abs. 1940, 34, 7291).

Isomerisation during cyclisations.

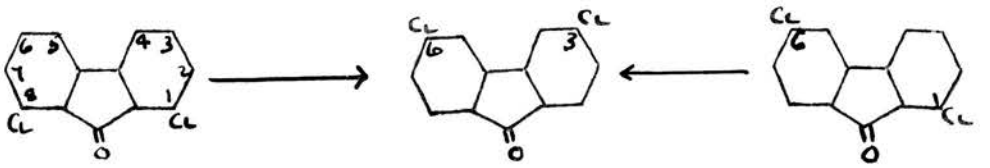
In a series of papers Huntress et alia have examined the formation of fluorenone-4-carboxylic acids from substituted diphenic acids. In the process, isomerisation during cyclisation, was discovered, e.g. 3;3' dichloro-

diphenic acid on treatment at 125°C. with conc. sulphuric acid gives 1:6-dichlorofluorenone-5-carboxylic acid while treating either 3:3'-dichlorodiphenic acid or 1:6-dichlorofluorenone-5-carboxylic acid with sulphuric acid at 170°C. furnished 1:6-dichlorofluorenone-4-carboxylic acid.

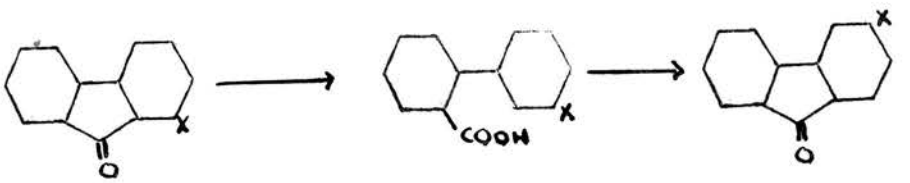
SCHEME 53



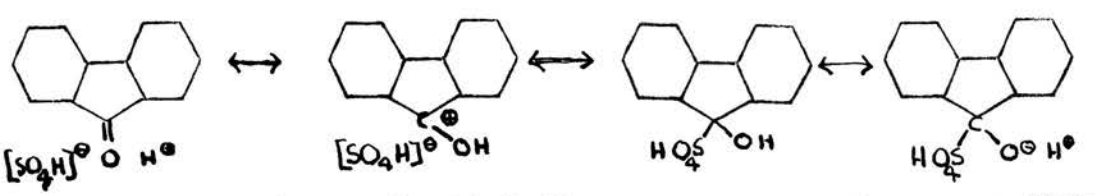
It was subsequently found that 1:6-dichlorofluorenone and 1:8-dichlorofluorenone rearrange in concentrated sulphuric acid on heating to give 3:6-dichlorofluorenone (Huntress and Atkinson, J.A.C.S., 1936, 58, 1514; Huntress, Cliff and Atkinson, J.A.C.S., 1933, 55, 4262).



Huntress and Seibel (J.A.C.S. 1939 61 1067) discussed the mechanism and suggested that a cleavage was involved as below.

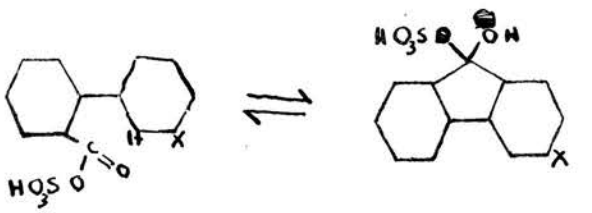


This explanation is insufficient as it ignores the function of the sulphuric acid, which cannot be replaced by phosphoric acid at least at the same temperature. It is improbable also that a fluorenone can be regarded as the true intermediate in the reaction as, in acids like sulphuric acid, it exists as an oxonium ion. This ion may be considered as a hybrid of several canonical forms, viz.



At the temperature at which the rearrangement occurs this oxonium sulphate must suffer an internal change involving effectively a transfer of proton to one of the benzene nuclei (probably as a hydrogen ion followed by an electron transfer). The sulphuric acid may serve a further function

by maintaining a high concentration of hydrogen ions as in the reaction sequence.

Oxonium sulphate 

The intermediate is represented here as a mixed anhydride of sulphuric acid and a biphenyl-2-carboxylic acid. At the temperature where the activation energy of the intramolecular change is available, the intermediate anhydride will be formed probably transitorily. When a substituent such as X above is present their will be effectively two different points at which cyclisation may recur — ortho or para to X. If, as in the cases investigated by Huntress et alia, there is any factor favouring para rather than ortho cyclisation, there will eventually be a greater amount of the para-cyclised product compared with ortho-cyclised product.

It is unfortunate that Huntress did not investigate the simpler 1- and 3-monosubstituted fluorenones but relied on the more readily available 1:8-dichlorofluorenone and 1:6-dichlorofluorenone. Where 1-substituted fluorenone derivatives are available, this reaction may prove of use for the synthesis of 3-substituted derivatives by interconversion from the 1-compounds. However, there was no

evidence (page 248) that treatment of fluorenone-1-carboxylic acid gives fluorenone-3-carboxylic acid.

(β)

The conversion of diphenic acid directly to fluorenone has been achieved in two ways:

(1) Heating with soda lime, or heating the calcium salt.

(2) Heating alone to 360°C.

(1) The first process was one of the classical procedures for the synthesis of fluorene derivatives. Where, however, the required diphenic acids were obtained from phenanthraquinones the method of Schmidt and Bauer (PAGE 113) has most often been used.

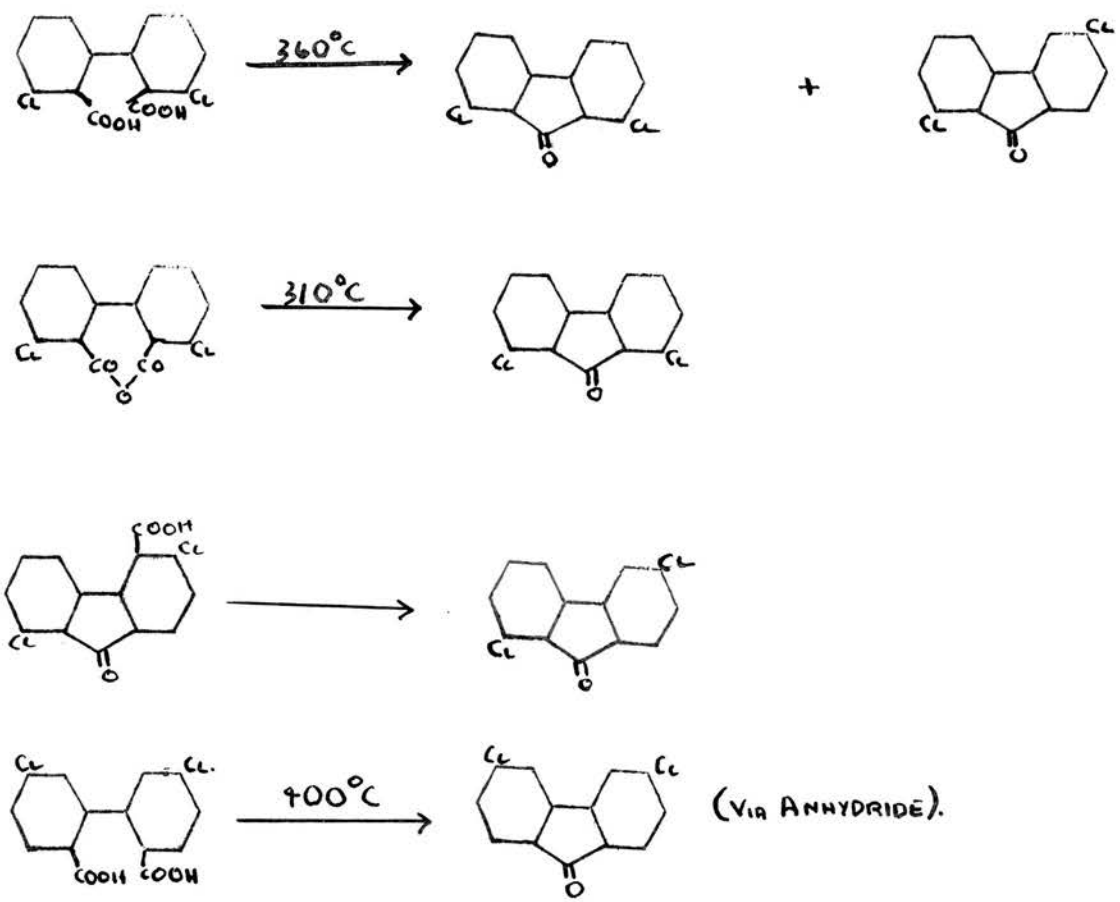
A typical example of this synthesis is the preparation of 2:7-dibromofluorenone from dibromodiphenic acid (Goldschmiedt and Schranzhofer, Monatsh., 1895, 16, 820; cf. Claus and Erler, Ber., 1886, 19, 3149; Courtot, loc.cit.).

More recently Huntress and Atkinson (loc.cit.) have prepared 3:6-dichlorofluorenone by heating the calcium salt of 5:5'-dichlorodiphenic acid.

(2) Huntress, Hershberg and Cliff (J.A.C.S., 1931, 53, 2720) reported that the heating of diphenic acid, diphenic anhydride and fluorene-4-carboxylic acid gives rise to fluorenone in good yield. Huntress and Cliff (J.A.C.S., 1933, 55, 2559)

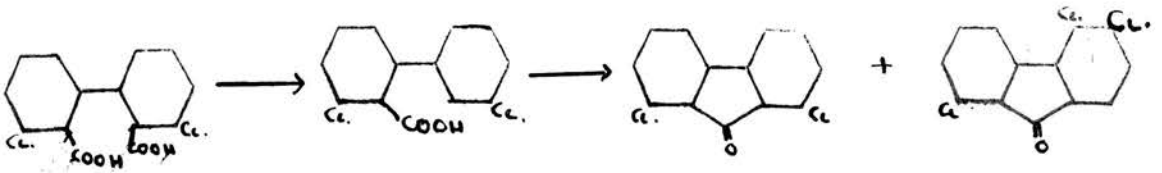
subsequently investigated the mechanism of this reaction. Their results are represented schematically below.

SCHEME 5E



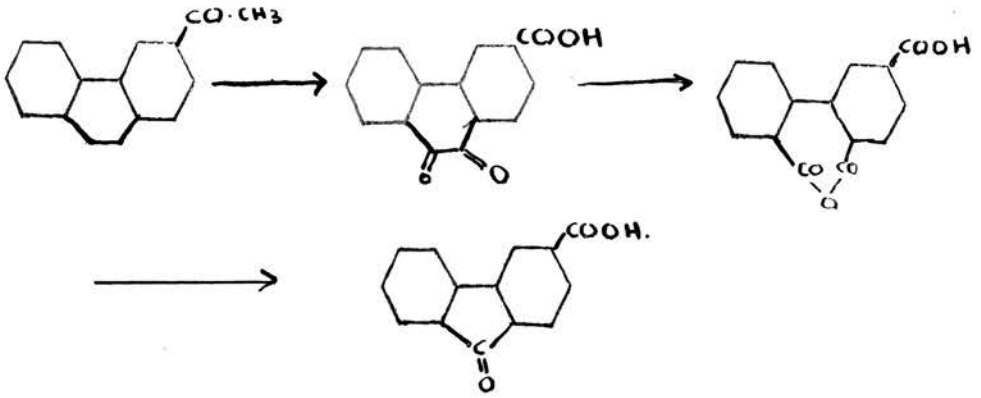
They concluded that either (1) The action of heat may follow either or both of the following courses (a) both the anhydride and the keto acid may be formed and each lose water to yield the 1:8 and 1:6 dichlorofluorenone; or (b) the intermediate monocarboxylic acid may form and subsequently lose water in two ways, one to yield the 1:8 ketone, the other to give the 1:6 ketone.

(2) The action of heat cannot involve the anhydride or the keto-acid alone but may involve the monocarboxylic acid alone.



This method of formation of fluorenones has not been exploited but - as long as the anhydride of the diphenic acid is used - it is potentially a useful synthetic method, e.g. the synthesis of fluorenone-3-carboxylic might have been more readily achieved by the process shown in Scheme 55 rather

SCHEME 55



than that described (page 269.).

(iii)

Syntheses from benzophenone or diphenylmethane derivatives

The syntheses are considered under the headings,

(1) The Ullman Synthesis.

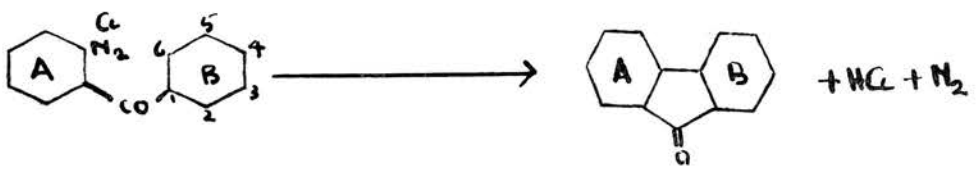
(2) The Work of Montagne.

(3) The Work of Kliegl and Vorländer.

(1)

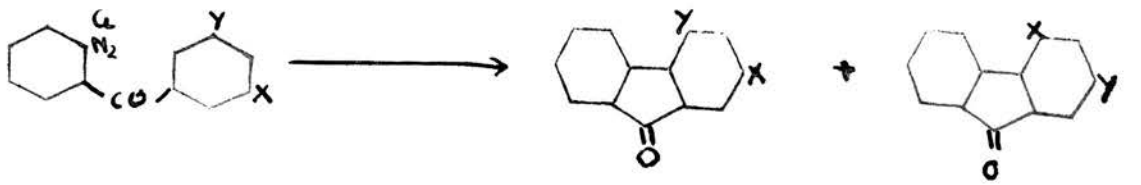
The Ullmann Synthesis

This synthesis is analagous to the Pschorr phenanthrene synthesis and consists of the decomposition of substituted benzophenone-2-diazonium chlorides.



Again the nature of the substituents decides whether the product will be a single substance or a mixture. Substitution in ring A does not affect the outcome of the reaction nor does a substituent in position 4 of ring B (corresponding to 3 in the resulting fluorenone). A substituent in position 2 of

ring B will lead to cyclisation in position 6 giving a 1-substituted fluorenone; a single substituent in position 3 or position 5 of ring B or two different substituents in 3 and 5 will lead to two products.



The method is therefore apparently especially adapted to the synthesis of

(1) 3-substituted fluorenones

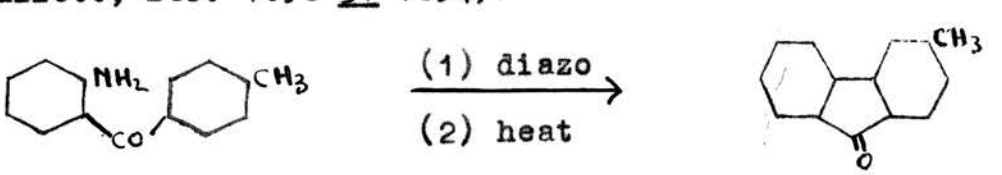
(2) 1-substituted fluorenones

(3) 2;4-disubstituted fluorenones in which the substituents are identical.

(4) Any fluorenone derivative derived from corresponding orthoaminobenzophenones substituted in ring A and containing substituents corresponding to conditions (1), (2) and (3) in ring B.

Of these (1) and (4) are the only cases especially used.

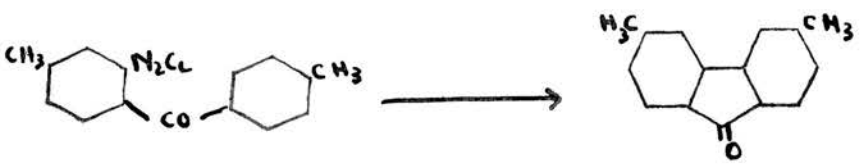
(1) <u>The synthesis of 3-methyl-fluorenone</u> (Ullmann and Mullett, Ber. 1898 <u>31</u> 1694).



(4) The synthesis of 1-bromofluorenone (Huntress, Pfister and Pfister, (loc.cit.) cf. Miller and Bachmann (loc.cit.))

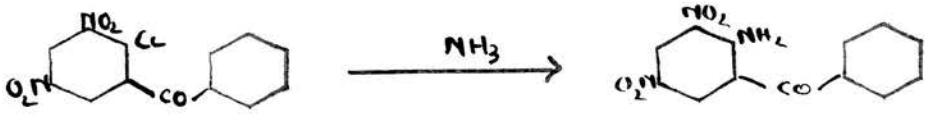
(4) The synthesis of 2:4-dinitrofluorenone (Ullmann and Broido, Ber., 1906, 39, 360)

(1) and (4) The synthesis of 3:6-dimethylfluorenone (Chardonnens and Wurmil, H.C.A., 1946, 29, 922)

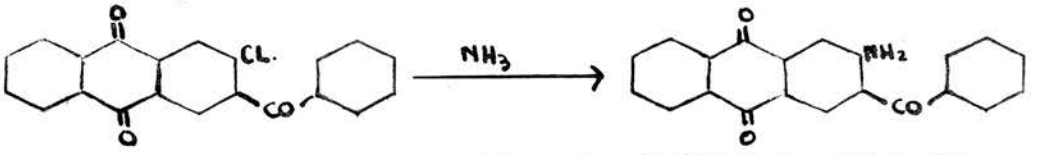


The synthesis of the required o-aminobenzophenones may be achieved by several routes. These — with one important exception—have been reviewed by Simpson, Atkinson, Schofield and Stephenson (J., 1945, 646). (See also page 254.) The exception is the use of the activating effect of groups such as nitro or benzoyl or halogen atoms ortho or para to them. On treating such halogeno compounds with ammonia

the halogen is replaced with an amino group, e.g. (1) Ullmann and Broido (loc.cit.) used this to obtain the required intermediate.



Ullmann and Dasgupta (loc.cit.) similarly used this method to prepare 2-amino-3-benzoyl anthraquinone.

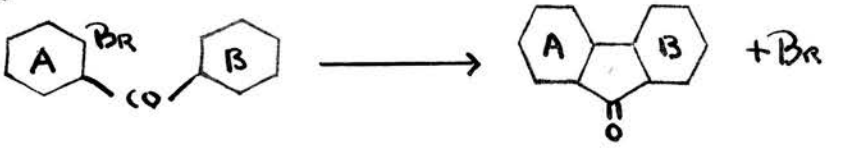


More recently Chardonnens and Perriard (H.C.A., 1945, 28, 593) Chardonnens and Wurmil (loc.cit.) and Chardonnens and Tienert (H.C.A., 1949, 32, 2340-8) have used analogous reactions to prepare nitro derivatives of 3-methyl and 3:6-dimethylfluorenone for comparison with the products of direct nitration of the alkyl and dialkyl fluorenone.

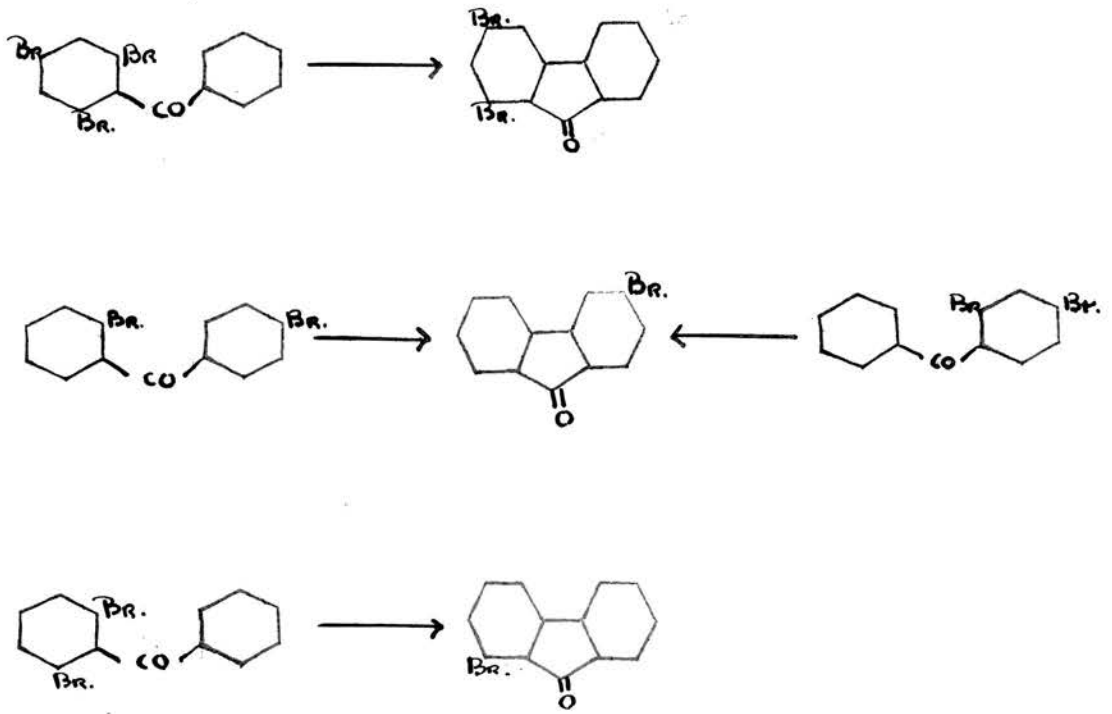
(2)

The Work of Montagne

Montagne (Rec., 1909, 28, 449) and Montagne and van Charante (Rec., 1913, 32, 164) examined the intramolecular dehydrohalogenation of substituted 2-bromobenzophenone with the formation of fluorenones



The same limitations apply as for the Ullmann Synthesis and Montagne prepared only compounds substituted in ring A or substituted in ring B in the 3-position thus

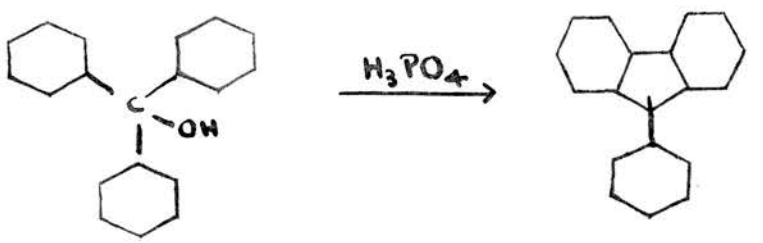


Although subsequent workers claimed difficulty in repeating this work the physical constants found by Montagne agree well with those for the same compounds derived from alternative syntheses.

(3)

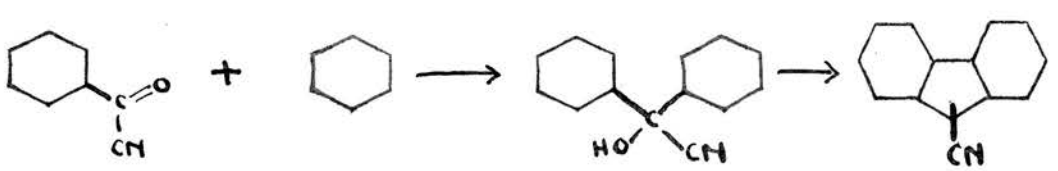
The Work of Kliegl and Vörlander

Kliegl (Ber., 1905, 38, 284) reported the formation of 9-phenyl fluorene by heating triphenylcarbinol with phosphoric acid. The yield was surprisingly good, viz. 40-50%



This reaction is limited in applicability for the introduction of different substituents into rings A, B & C would lead to complications.

Vorländer and Hüth (Ber., 1911, 44, 2466) reported the synthesis of fluorene-9-nitrile by the reaction of benzoyl cyanide with benzene in the presence of aluminium chloride. (Yield 0·8 gms from 3 gms benzoyl cyanide.)



In a subsequent paper Vorländer and Pritzche (Ber., 1913, 46, 1793) prepared fluorene-9-carboxylic acid from benzilic acid.

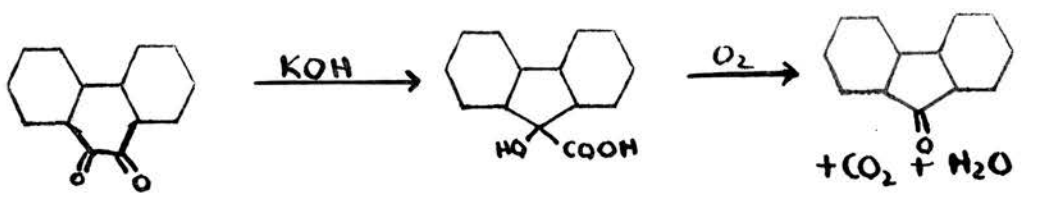
(20 gms benzilic acid $\longrightarrow$ (9 $\longrightarrow$ 10) gms product.)

This method has received little application although its limitations are similar to those for the other syntheses from derivatives of diphenylmethane and benzophenone.

(iv)

Synthesis from phenanthraquinones

This method, which was extensively applied by Schmidt and Bauer (Ber., 1905, 38, 3737; Ber., 1905, 38, 3758) consists in the treatment of phenanthraquinones with alkali when a benzilic acid rearrangement occurs with a decrease in ring size of the central ring. The products are 9-hydroxy 9-carboxy fluorenes which may readily be oxidised to the corresponding fluorenones



Mention has previously been made of uses of this synthesis (pages 4 Note) which has probably been the most fruitful method for the synthesis of 2-, 2:7- and 4-substituted fluorene derivatives. Its more general applicability has been limited by the difficulty of obtaining the required

phenanthrene derivatives. However, Schmidt and Soll (Ber., 1908, 41, 3691) synthesised 3-nitrofluorenone successfully by this method from 3-nitro-phenanthraquinone.

(v)

Syntheses from hydrindene derivatives

The synthetic methods employed are considered under the headings

(1) Diene reactions using indene as dienophile or 3-vinylindene derivatives as nucleophile.

(2) Condensation reactions of ketonic derivatives of hydrindene.

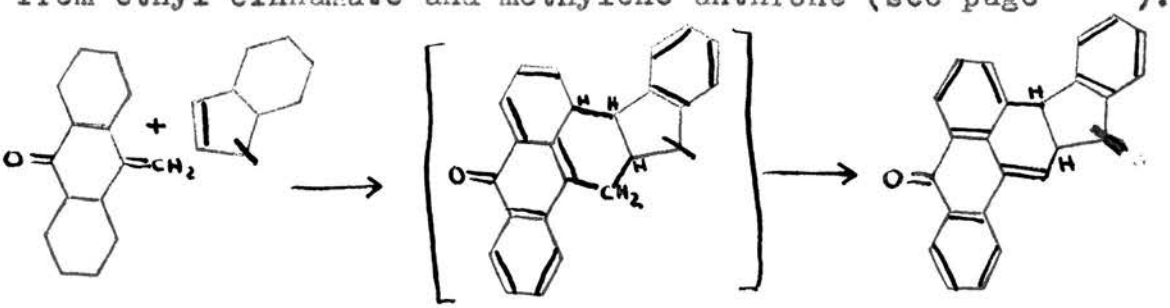
(1)

Diene Reactions leading to Fluorene derivatives

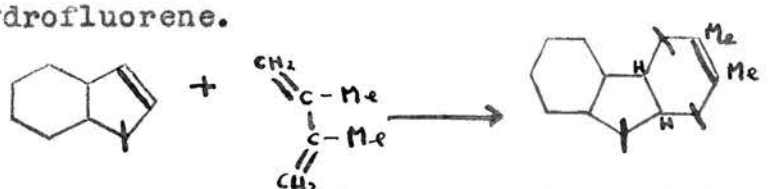
Swain and Todd (loc.cit.) and Alder and Rickert (Ber., 1938, 71, 384) have used indene as a dienophile in diene reactions leading to fluorene derivatives.

(a) On condensing indene and 9-methyleneanthrone derivatives of indeno-2":3"; 2':1'-benzanthrone were obtained. Depending on the solvent used either (a) both the indeno-2":3"; 2':1'- and its dihydro-derivative were obtained (solvent nitrobenzene) or (b) the dihydro-derivative was obtained alone (benzene and xylene). On refluxing in nitrobenzene a partial conversion of the dihydro-derivative to the indenobenzanthrone occurred. In no case could a tetrahydroindenobenzanthrone be isolated.

Oxidation of the indeno-2":3"; 2':1'-benzanthrone led to the 1"-keto-indenobenzanthrone which was identical with the product obtained from ethyl cinnamate and methylene anthrone (see page).

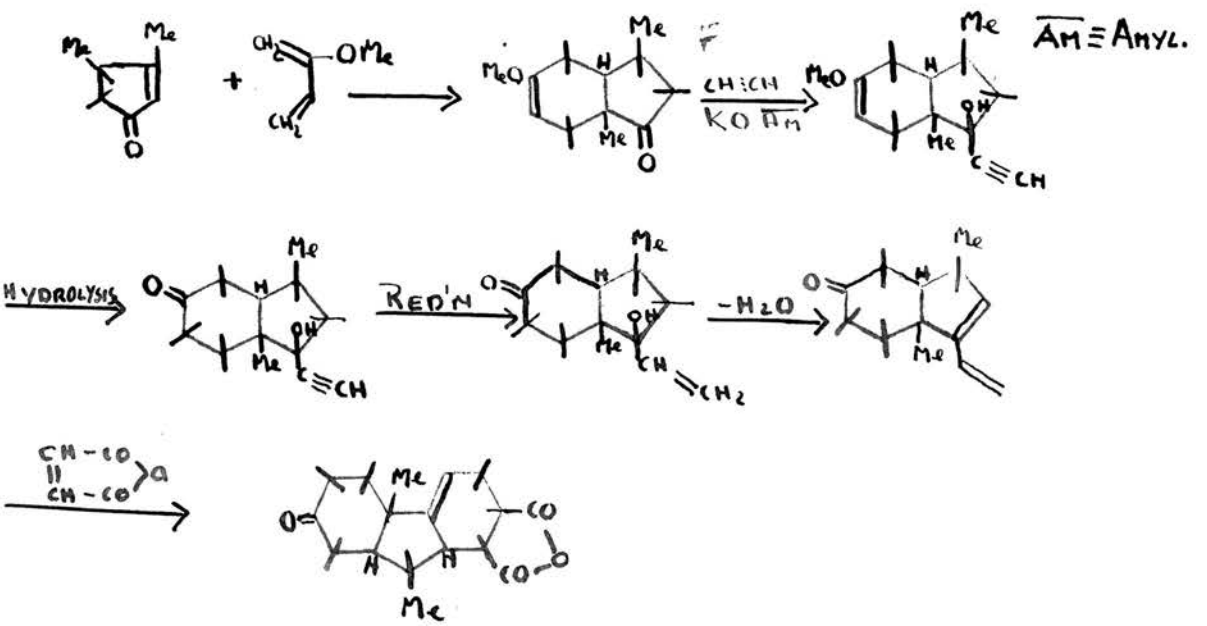


(β) Alder and Rickert condensed indene and 2,3-dimethyl-butadiene and thus obtained 2,3-dimethyl-1,4,4a,1a-tetra-hydrofluorene.

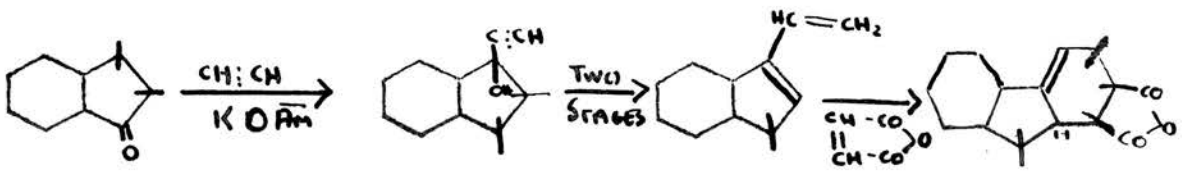


Nazarow, Bergelson, Shmonina and Terekhova (Abs., 1950, 44, 3458) synthesised a complex dimethylketo-decahydro-fluorene dicarboxylic acid by the scheme shown below.

SCHEME 56



The important feature of this reaction sequence is the applicability of the last few stages to say hydrindone, e.g.

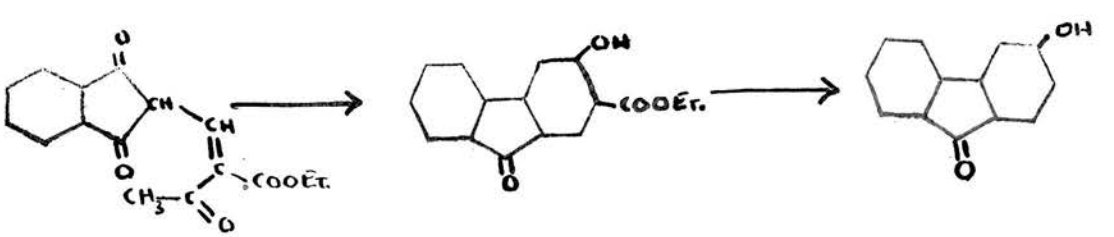


(cf. Dane, Höss, Bindseil, and Schön, Ann., 1937, 532, 39.)

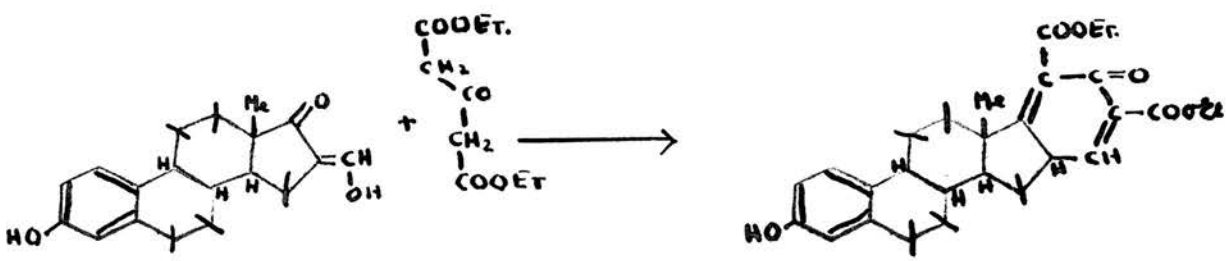
(2)

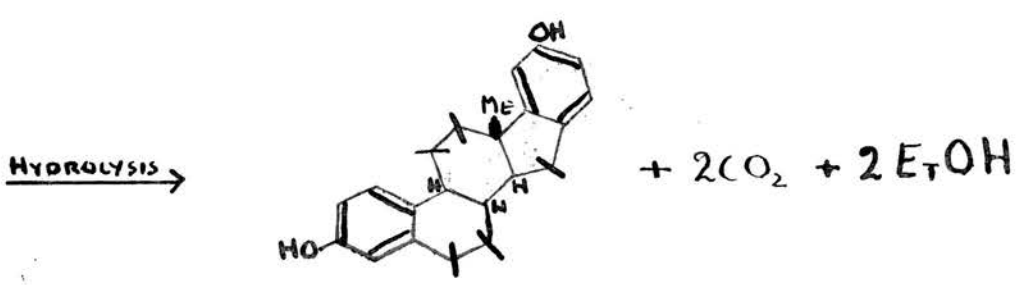
Condensation Reactions of Ketonic derivatives of Hydrindene.

(1) Emera and La Spada (Gazz., 1905, 35, (2), 539) synthesised 3-hydroxyfluorenone-2-carboxylic acid from ethyl-1:3-diketo-hydrindene-2-methenylaceto-acetate (Emera and Casardi, Gazz., 1905, 351[1],1) by the action of alkali. On decarboxylation the 3-hydroxyfluorenone-2-carboxylic acid gave 3-hydroxy-fluorenone (cf. Ullmann and Bleier, loc.cit.).



(2) Ruzicka, Prelog and Battegay (H.C.A., 1948, 31, 1296-1301) reported a synthetic method originating from α-oxymethylene ketones of the steroid series which gave rise to complex derivatives of fluorene. There is no reason why it should not be applied to simpler derivatives of hydrindene, e.g.





SECTION IV

THE MILLS NIXON EFFECT

(1)

THE MILLS NIXON EFFECT

Mills and Nixon (J.,1930, 2510) pointed out that if the angle between the two single bonds of a doubly bound carbon atom is equal to the tetrahedral angle (109·3°) then the angle which the single bonds make with the plane of the double bond would be 125·3°. Now both these angle sizes differ markedly from the angle size normally associated with a benzene ring, viz. 120°C. fig. I .

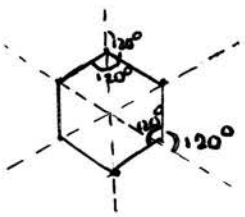


Fig. I.

Fig. II (a).

Mills and Nixon investigated the effect of fusing an alicyclic group to two ortho positions of a benzene ring. They concluded that in hydrindene the strain in the trimethylene group would be least if the common linkage of the fused rings was a single bond and that in the case of tetralin there would be less strain if the common linkage was a double bond. They postulated that for both hydrindene and tetralin the equilibrium between the two Kebulé forms

for each would favour the form which possessed less strain, fig.

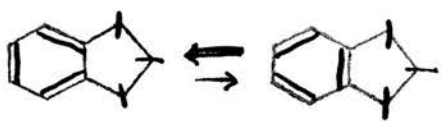
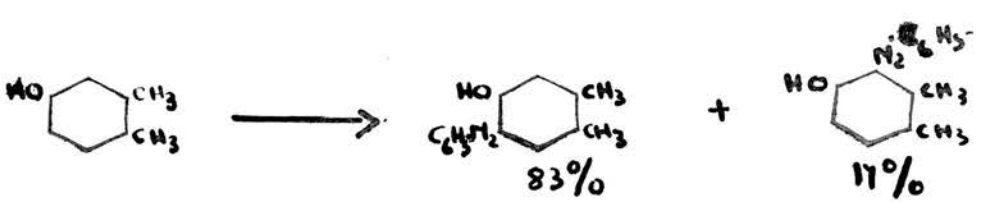


Fig. II (b).

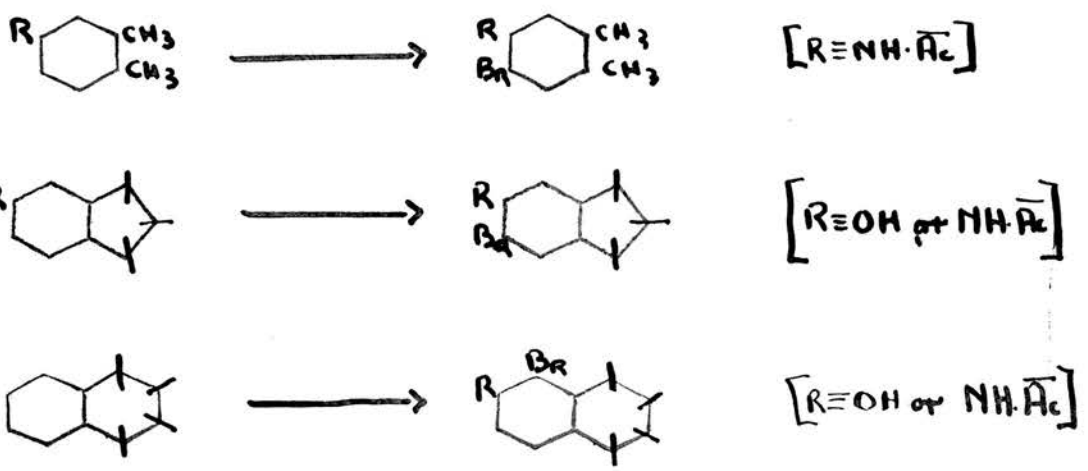
Fig. II (c).

To justify these suggestions they examined the reactions of corresponding derivatives of o-xylene, hydrindene and tetralin for differences that might reasonably be assumed to be due to any stereochemical effect of the ring system. They felt that it was permissible to conclude that the differences in the nature of the side chain would not, for any other reason than its stereochemistry, affect the reactivities. The reactions that they discussed were:

(i) <u>Coupling of phenols with benzene diazoniumchloride</u>



(ii) Bromination of Phenols and acetamido compounds



They inferred that in 1:2-dialkyl-4-phenols the more stable arrangement of bonds in the benzene ring is shown in fig. III , and that the arrangement in the case of hydrindene is normal and in the case of tetralin abnormal.

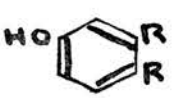


Fig. III.

Sutton and Pauling (Trans. Far. Soc., 1935, 31z 939) interpreted the Mills Nixon suggestion in terms of the resonance theories and showed that in hydrindene and tetralin the trimethylene and tetramethylene groups do not radically affect the resonance energy of the benzenoid ring. This conclusion has been confirmed experimentally for hydrindene (Brockway and Taylor, loc. cit; vide page 16.).

Sidgwick and Springall (J., 1936, 1532) attempted to confirm the conclusions of Mills and Nixon by dipole moment studies using 5;6-dibromohydrindene and 6;7-dibromotetralin, o-dibromobenzene and 4;5-dibromo-o-xylene. They concluded that there is in hydrindene a fixation in the correct sense but in tetralin there is no fixation. The truth of this can only be accepted if the fundamental assumptions of Sidgwick and Springall are correct.

Criticisms

(1) They use the van't Hoff model for the ethylenic bond in calculating the probable bond angles; Mills and Nixon had, however, accepted this model as only qualitatively correct.

(2) There are several inconsistencies in this paper which deserve comment mostly from the point of view of possible experimental error.

(a) In examining the monohalogeno compounds the following results were obtained (Table I.).

TABLE I.

Compound	Calc. Moment	Observed Moment	Δ
6-Bromotetralin	2·12	2·23	0·11
Hydrindene	2·08	2·15	0·07
o-Xylene	2·10	2·07	0·03

(b) In examining the dihalogeno compounds the following results were obtained (Table 2).

TABLE 2

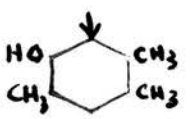
Compound		Calculated Moment	Observed Moment	Δ	
6;7-dibromotetralin	(a)	2·21→2·30	2·11	0·1	0·2
	or (b)	2·12	2·11	0·01	
5;6-dibromohydrindene	(a)	1·99→1·84	1·78	0·06	0·21
	or (b)	2·12	1·78	0·34	
4;5-dibromoxylene		2·12	2·13	0·01	

(a) Calculated for fixation (b) calculated for no fixation.

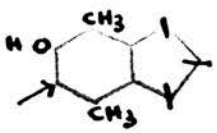
If Table 1 gives an indication of the order of error then in Table 2 the results for dibromotetralin are inconclusive, for if the error in Table 1 is of the order 0·06→ 0·1 then the results for dibromohydrindene and dibromotetralin both fall short of the values calculated for bond fixation by roughly comparable quantities. If the error is smaller than the limits discussed then Sidgwick and Springall must discard their models for 5;6-dibromohydrindene as their observed moment does not fall within the limits calculated from their models.

Sidgwick and Springall's work must be treated with caution as they have not assessed the experimental errors involved.

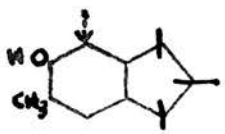
Fieser and Lothrop (J.A.C.S., 1936, 58, 2050; ibid., 1937, 59, 945) and Lothrop (ibid., 1940, 62, 132) applied some of the methods which had been used successfully in the studies of the fine structure in the naphthalene series. They examined the coupling reactions of some o-alkylphenols of the hydrindene, tetralin, and o-xylene series, with substituted benzene-diazonium chloride.



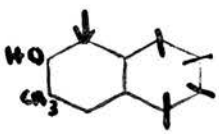
Couples, 1.



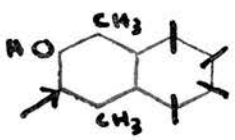
Couples, 2.



Couples in lower yield, 3.



Couples, 4.



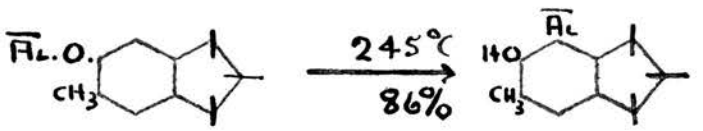
Couples, 5.

Compound 3 above was at first thought to resist coupling but it was later shown that the coupling reactions were sensitive to pH, Table 3 .

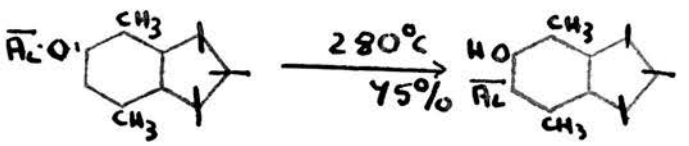
TABLE 3

Compound	pH	Yield	Yield in 4NNaOH
β-naphthol	7·5	95%	4·0%
3	7·5	69%	0·5%
2	11·3	69·5	5·7
3	11·3	68·7	0·5
5	11·3	55·5	7·0

Similarly in the Claisen rearrangement of the allyl ethers of 2 and 3 above both reacted easily.



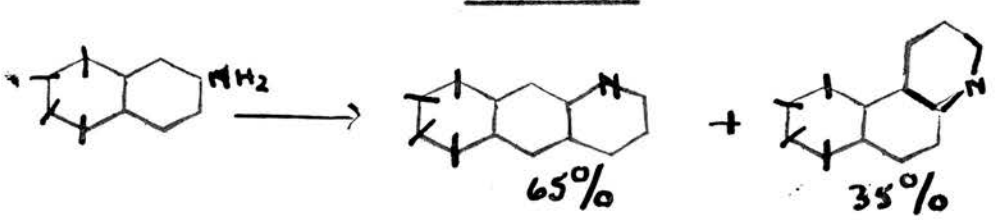
$\overline{A_L} = CH_2-CH=CH_2$

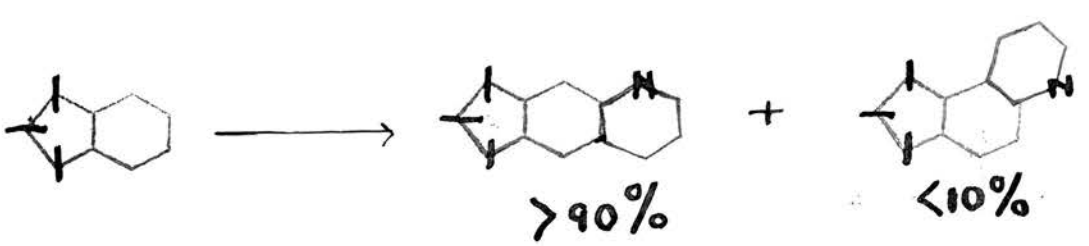


It was concluded by those workers that no bond fixation comparable to that found in the naphthalene series exists in the case of hydrindene.

Lindner, Sellner, Hofmann and Hagen (Monatsh., 1939, 72, 337) examined the Skraup reactions of 5-amino-hydrindine and 6-aminotetralin. Their results are summarised in Scheme 57.

SCHEME 57





It is obvious that in the case of 5-aminohydrindene the reaction proceeds in the manner that would have been predicted on the Mills Nixon theory. In the case of 6-aminotetralin however the mixture, although it contains relatively large proportions of both isomers, contains a larger proportion of the isomer whose production, by prediction from the Mills Nixon theory and by analogy with the coupling reactions, would be expected to be disfavoured.

Sandin and Evans (J.A.C.S., 1939, 61, 2916) examined the reduction of 4:6-dibromo-5-aminohydrindene and 4-bromo-5-aminohydrindene. The lability of the bromine atom in the 6-position was greater than that in the 4-position.

4:6-dibromo-5-aminohydrindene $\xrightarrow{0\cdot5 \text{ hours}}$ 80% 4-bromo-5-aminohydrindene

4-bromo-5-aminohydrindene $\xrightarrow{6 \text{ hours}}$ 25% unchanged material

Similar experiments with 5-bromo-6-aminotetralin demonstrated the lability of the halogen in the 5-position. The importance of this work is that in similar experiments in the naphthalene series where a large degree of double bond fixation exists it was found that in o-halogenoamino-naphthalenes the greater the double bond character of the separating bond then the greater would be the lability of the bromine. They concluded that the preferred structures for the hydrindene derivatives are based on the Mills Nixon formulation.

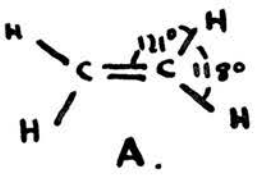
Arnold and Evans (J.A.C.S., 1940, 62, 556) reviewed the subject and showed the invalidity of the two fundamental

postulates of Mills and Nixon.

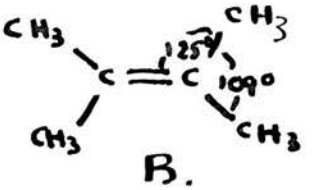
(i) The structure of the double bond is not that of the van't Hoff model.

(ii) The existence of a simple relationship between bond type and bond angles is untenable.

The true structure of ethylene is A below (Thompson, Trans. Far. Soc.,1939, 35, 697) and in the opposite extreme Pauling and Brockway (J.A.C.S.,1937, 59, 1223) have shown that the angles of tetramethylethylene are nearly tetrahedral B.



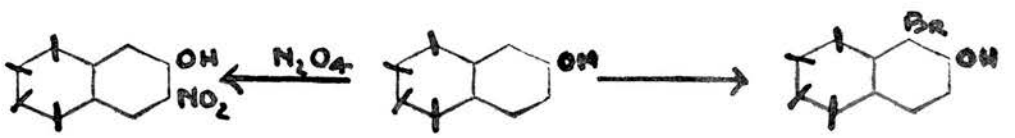
A.



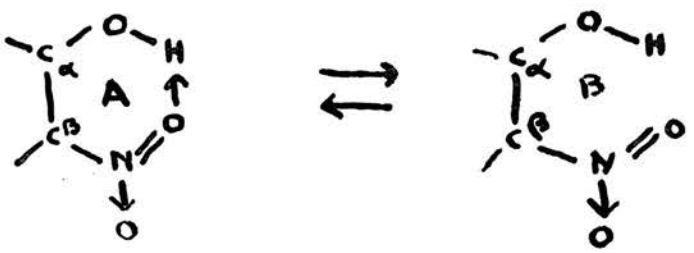
B.

The simple correlation of bond angle and bond type appears to be unacceptable and it is on this erroneous basis that Sidgwick and Springall's calculations are founded.

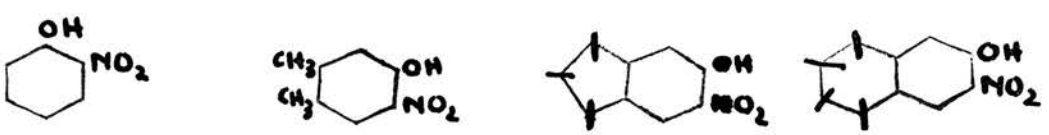
They pointed out further that no reliance could be placed on the results of substitution reactions with high activation energies and on this basis the explanation of the apparent contradictions in the reactivity of 6-hydroxytetralin is laid.



To avoid this difficulty Arnold and Evans investigated physical measurements which might show vital differences between tetralin and hydrindene derivatives. The first method was an investigation of the acidity of o-nitro-phenols which depends on the stability of the chelate ring.



If the bond $\alpha\beta$ is a stabilised double bond then the form A is favoured with a corresponding reduction in the acidity of the compound. They considered the 6 compounds below in order to assess the effect of substituents on the bond type of $\alpha\beta$; they realised however that the method had severe limitations and they kept, as far as possible, all factors other than the substituents constant.



(1') (2') (3') (4')

(5') (6')

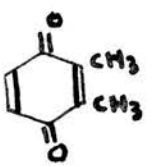
TABLE 4

Compound	T°C	pK
1'	29	8·2
2'	28	8·81
2'	37	8·90
3'	37	8·96
4'	37	9·05
5'	28	8·57
6'	28	8·43

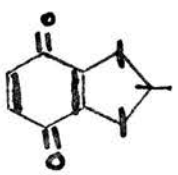
The similarity between the pK values for 2,3 and 4 indicated that there is no difference in bond order in these compounds.

The most obvious criticism of the sensitivity of this work is that small differences in the bond order due to substituents would have little effect on the acidity because of the great and decisive resonance stabilisation of the chelate structure which is a naphthalene analogue. Arnold and Zaugg (J.A.C.S., 1941, 63, 1317) realised that insensitivity existed and approached the problem from an alternative facet by considering the oxidation/reduction potentials of o-xyloquinone, 4:7-hydrindenequinone and 1:2:3:4-tetrahydro-naphthoquinone-5:8. Any geometric strain in the hydrindene-quinone, i.e. a positive Mills Nixon effect, could be relieved by reduction to the benzenoid nucleus accompanied

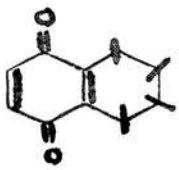
by partial stabilisation. This being the case hydrindene quinone would be expected to have a higher oxidation potential than either of the others. This is in fact the case and a Mills Nixon effect must be present.



(1)



(2)

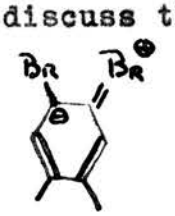


(3)

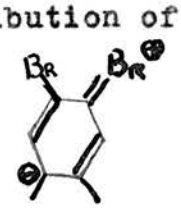
	Oxidation Potential
(1)	0·588
(2)	0·641
(3)	0·585

Kossiakoff and Springall (J.A.C.S., 1941, 63, 2223) pointed out that the reactions, on which conclusions concerning the Mills Nixon effect are based, progress essentially through an excited ionic structure of the molecule which has a free electron pair at the position being attacked. Any conclusions derived from the reactions should be applied to the excited state.

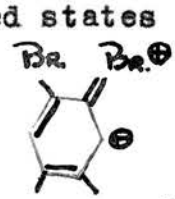
These workers examined the electron diffraction of o-dibromoxylene, o-dibromohydrindene and o-dibromotetralin and they discuss the contribution of such excited states as



A



B



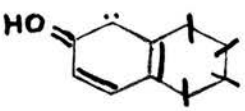
C

etc.

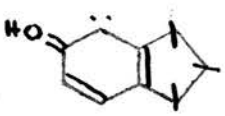
A and B possess single bonds at the junction and the Mills Nixon effect affects the stability and therefore the contribution of such structures. They concluded that the total contribution of such ionic states would be greatest in o-dibromohydrindene and least in o-dibromotetralin and that the positions of substitution are dependent on the relative excitation energies of A and C.

Pullmann (Bull Soc.,1947, M337) examined the problem from a theoretical standpoint and his conclusions which resemble those of Kossiakoff and Springall are outlined in Scheme 58 below.

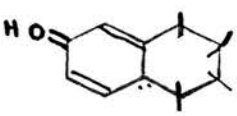
SCHEME 58



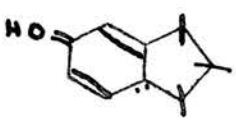
Most Important



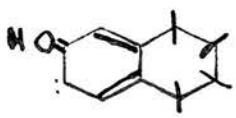
Contributes little because of M.N. effect.

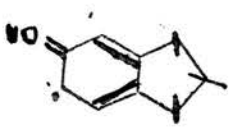


Less Important



Contributes to resonance hybrid but unimportant in reaction.



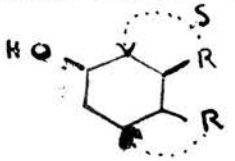


Most important

In the case of o-xylene the deciding factor is the para directing influence of the methyl group.

The problem of the Mills Nixon effect has not been acceptably or convincingly solved. The evidence of substitution reactions is so confusing that by a judicious choice hydrindene and tetralin may be shown to possess bond fixation in the same sense. The principal difficulty is that the theoretical interpretation of substitution reactions in aromatic molecules is highly complex. In considering, for example, the substitution reactions of certain of the phenols discussed above the following factors must be considered.

(1) The steric effect of the alkyl groups



This will favour the unhindered position para to the alkyl group.

(2) The directing influence of the alkyl groups

This will favour the free position para to one alkyl group rather than the ortho positions to the alkyl groups.

(3) The directing effect of the phenolic group.

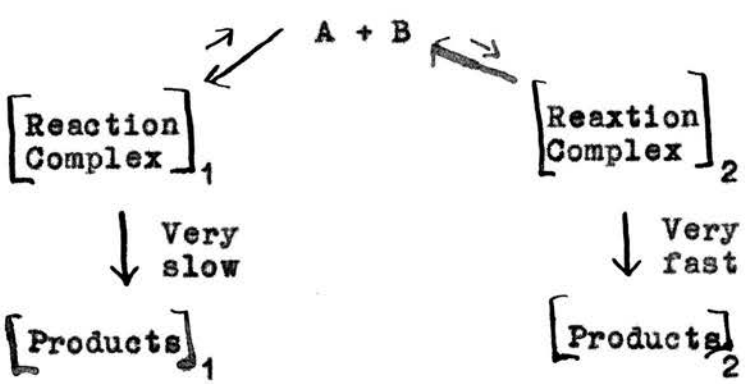
This favours equally the two ortho positions if condition (4) is the same for both ortho positions.

(4) The transmission of directing effects to two ortho positions will be dependent on the double bond character of the bonds joining the two ortho positions to the carbon atom carrying the phenolic group.

(5) The thermodynamic factors, e.g. the activation energies of the reactions and the relative energies of the various possible products, will control the outcome of any substitution reaction.

(6) The nature of the entering substituent group will affect markedly the final product for, if the reaction occurs via a reaction complex, the nature of the starting materials will control the formation of the possible reaction complexes but the decisive factor may be the rate of decomposition of the various complexes. In Scheme 59 $[\text{Products}]_1$ may be formed in only a small quantity relative to $[\text{Products}]_2$.

SCHEME 59



To all these must be added a further factor, namely the Mills Nixon Effect. The work of Arnold and Zaugg has shown that if, as happens in the quinones studied, a double bond exists at the point of fusion of a five-membered ring with a 6-membered ring, then a lower stability, relative to compounds which are unfused or possess 2 fused 6-membered rings, occurs. This proves the original Mills Nixon postulate but it is impossible to prove it by chemical means for any cases other than those where the effect is highly exaggerated as in the quinones. The first 3 factors and the Mills Nixon effect can safely be regarded as individually interpretable but any failure to interpret correctly the course of a substitution reaction must be blamed on the complex balance and interdependence between all the factors controlling the reaction process, and especially (4), (5) and (6) which cannot at present be assessed. It must be remembered that (4), (5) and (6) are highly dependent on reaction conditions, and the nature of the reactants.

The success of Fieser, Lothrop et alia in their work on bond fixation in naphthalene and other condensed polycyclic hydrocarbons is due to the high degree of bond fixation in these substances. This causes large differences in the transmission effects to ortho positions to hydroxyl and amino groups and also in the thermodynamic effects; but even in this series examples may be quoted of minor alterations

in the reaction conditions which seriously affect the specificity of a reaction process which may have two possible courses; indeed complete reversal of specificity may at times be achieved.

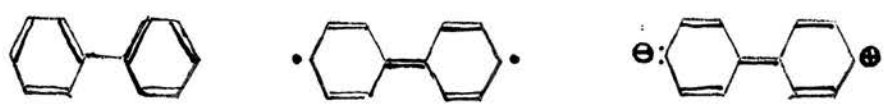
Although it is probable that the Mills Nixon effect is qualitatively existent its contribution to the final properties of simple benzenoid derivatives of hydrindene is almost certainly extremely small. The principal evidence of this is the high resonance stabilisation energy of hydrindene and the evident similarity between the absorption spectra of such compounds as o-xylene and hydrindene. The only apparent difference in the absorption which may be interpreted as the effect of a five-membered ring on a benzenoid ring is the resolution of the absorption curve of hydrindene into several discrete maxima. This will be discussed further in the next sub-section.

FINE STRUCTURE IN THE FLUORENE SERIES

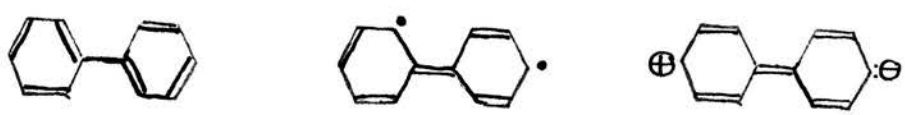
The fine structure of fluorene is discussed in comparison with biphenyl, toluene and naphthalene.

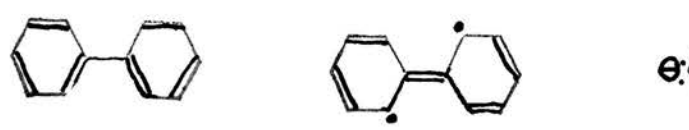
Fluorene and biphenyl. The resonance energy of biphenyl exceeds that possessed by a simple benzenoid structure by 8K. cals./mols. (Pauling and Sherman, J. Chem. Phys., 1933, 1, 606); this indicates marked interaction between the two benzenoid rings and this may be represented by several canonical structures which contribute to the resonance and which are diradical or dipolar.

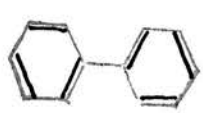
e.g. Normal Diradical Dipolar



Most significant Diradical

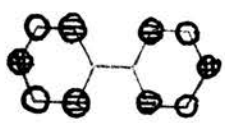




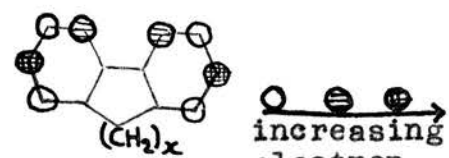


Etc. Etc.

It is probable that the normal canonical forms are the most significant contributors followed by the diradical forms. It is unlikely that the dipolar forms play any large part in the resonance. The resulting hybrid may be represented by the structure A.



A



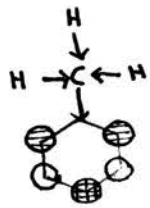
B

This may be described in Pullman's terminology as follows:

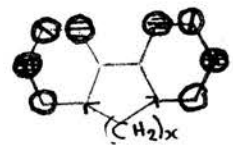
"'Peaks' exist in the electron distribution contours at the 4, 4' positions and lesser peaks at the 2, 2', 6, 6' positions".

By analogy the reactivity and structure of the polymethylene biphenyls may be represented as a first approximation by B.

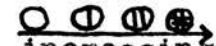
Fluorene and toluene. The dipole moment and chemical reactivity of toluene are now interpreted on the basis of structure C.



C

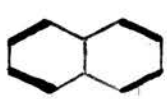


B'

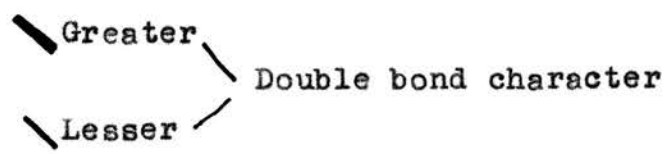


The methyl group and the phenyl group form a hyperconjugated system and 'peaks' exist strongly in the para position and less strongly in the ortho positions. When this effect is applied to the polymethylene biphenyl series a second order effect will be introduced and a closer approximation to the structure will be given by B'. This is the effect responsible for differentiation between positions 3 and 1.

Fluorene and naphthalene. The chemical and physical evidence agree that the fine structure of naphthalene may be represented by D.



D



The substitution reactions of naphthalene itself cannot be interpreted on such a structure alone for the

reactions of hydrocarbons are controlled by

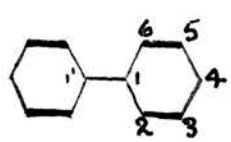
(1) the availability of electrons at the possible reaction sites under the reaction conditions.

(2) the mechanism of the reaction.

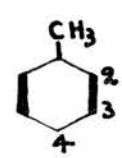
(3) the nature of the other reactants.

In naphthalene the 'α' and 'β' positions both possess considerable reactivity and the fine structure, i.e. variation in bond order, is of secondary importance in conditioning the outcome of the initial substitution but is of primary importance in further substitution by virtue of the differing capabilities of bonds, according to their character, to transmit the directing effects of the initial substituent. This is the basis of the analysis of the reactions of β-substituted naphthalenes on which the chemical evidence for the naphthalene fine structure is founded. How far must bond order differences be taken into account in the fluorene series?

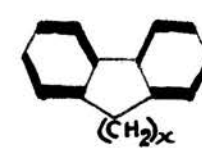
In the case of biphenyl itself it seems reasonable to indicate the differences in bond order by structure A'



A'



C'



B"

If there was no interaction between the six-membered rings then all the bonds, apart from 1, 1' which would be a true single bond, would be of identical type as in benzene. However interaction does occur so bond 1,1' has some double bond character and from the symmetry of the molecule bonds 2,3; 5,6; 2'3'; 5'6'; must differ from the rest in a manner dependent on the contribution of the first listed diradical canonical structure and the first and second dipolar canonical structures (page 135). As these contribute only slightly to the resonance hybrid the differences in the bond character will exist, as indicated, but will be of a small degree. In the case of toluene similar reasoning prevails and structure C' is the most likely representation but the differences between 2,3; and 3,4; will be very slight. When these conclusions are together applied to the polymethylene biphenyl structure, B" results in which a slight difference exists between bonds 1,2 and 2,3.

This analysis is extremely incomplete for it is impossible to assess by such qualitative arguments the interaction of these effects whose resultant truly represent the chemical and physical nature of fluorene and the other polymethylene biphenyls. It however suffices to show that the interpretation of the substitution reactions of fluorene and all the other

related hydrocarbons may be resolved into fairly simple terms. The many attempts that have been made to discuss the chemistry of fluorene by strict analogies with indene and cyclopentadiene and with reference to bond fixation in the naphthalene sense are unfortunate and misleading, principally because the comparisons are based on fallacious premises. As much information can be obtained from a comparison of fluorene, indene and cyclopentadiene as from the comparison of biphenyl, styrene and butadiene. The comparison of fluorene and naphthalene fails because the degree of bond fixation is completely different in each case and is not the same controlling factor in fluorene as in naphthalene chemistry. Fluorene must be dissociated from hydrocarbons containing condensed aromatic systems if it is to be satisfactorily considered.

"STEREOCHEMISTRY IN THE FLUORENE SERIES"

The difficulties in interpreting the distribution of the carbon atoms of fluorene in space according to the accepted tenets of the stereochemistry of aromatic hydrocarbons have led various workers (e.g. Cook and Iball, Chem. and Ind., 1936, 55, 67) to propose a non-planar formulation for fluorene. The difficulties involved are discussed and the shortcomings of a non-planar formulation are pointed out in this section; a new interpretation based on a planar structure is considered on the basis of the existing evidence together with possible routes to its confirmation.

In the following discussion the criterion of planarity of a hydrocarbon is that the centres of all the carbon atoms in the nucleus should be coplanar. It is now generally accepted that differences may exist in the bond lengths within six-membered aromatic rings but certain attendant implications have been ignored. The angle of 120°, the internal angle of the benzene ring, has been applied indiscriminately by organic chemists to all benzenoid structures without justification and this value must no longer be considered as sacrosanct. It must be admitted that the differences in the commoner hydrocarbons are not large but they must exist wherever

certain symmetries with regard to bond length are absent. Four examples of symmetries which do permit all the bond angles to be 120° are outlined below.

(1) If all the bond lengths are equal the internal angles may all be 120°.

(2) If alternate bond lengths in a six-membered ring are equal then the internal angles may all be 120° (fig I).

(3) If the lengths of opposite bonds are equal then all the internal angles may be 120° (fig.II).

(4) If three neighbouring bonds have lengths 'a', and two others, not neighbours, length 'b', then all the angles may be 120° if $\frac{b + c}{2} = a$ where 'c' is the length of the remaining bond (fig.III).

Proofs are given for 2 and 4 as 1 and 3 are apparent. It is obvious that if all the angles are 120° then opposite bonds must be parallel, so to establish the possibility of all the bond angles being 120° under the conditions of bond length imposed this parallelism must be assumed.

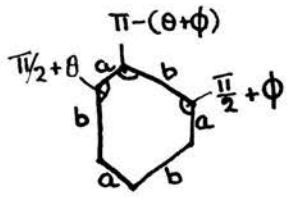


fig. I

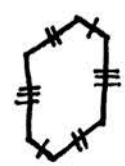


fig. II

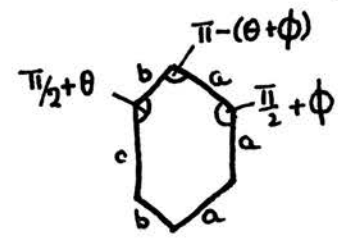


fig III.

Proof of (2). From fig. I $b + 2a \sin\theta = a + 2b \sin\phi$

If $\theta = \phi = 30^\circ$, i.e. if all internal angles are 120°, this equation resolves into the apparent equality $b + a = a + b$. Hence the validity of (2).

Proof of (4). From fig. III $c + 2b \sin\theta = a + 2a \sin\phi$

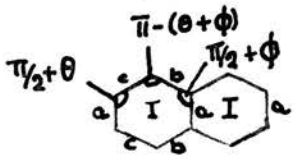
If $\theta = \phi = 30^\circ$

Then $c + b = 2a$

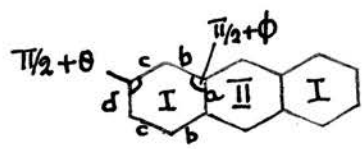
$\therefore \quad a = \frac{b + c}{2}$ if all internal angles are 120°.

Hence (4) is proved.

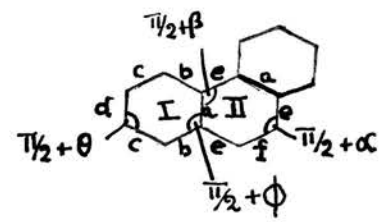
Such symmetries are not so very common and in naphthalene, anthracene (except ring II) and phenanthrene they do not appear to exist



$a \neq b \neq c$



$a \neq b \neq c \neq d$



$a \neq b \neq c \neq d$ and $a \neq e \neq f$

In each hydrocarbon the bonds which are closely similar in length are shown and their lengths designated by the same letter. The internal angles of the rings I are $(\pi/2 + \theta)$, $(\pi - (\theta+\phi))$ and $(\pi/2 + \phi)$ as shown.

Napthalene. From simple trigonometry it follows that

$$a + 2c \sin\theta = a + 2b \sin\phi$$

$$\therefore \sin\theta / \sin\phi = b/c \qquad \ldots(1)$$

Now $b > c$ $\quad\therefore \theta > \phi$

θ and ϕ although different are not far from 30° so an approximate value for $\theta - \phi$ can be obtained by assuming $\phi = 30^\circ$ and giving 'b' and 'c' the values found by Robertson, Abrahams and White (Acta Crystallographica, 1949, 2, 43), viz. b = 1.42Å & c = 1.36Å, in their crystallographic work.

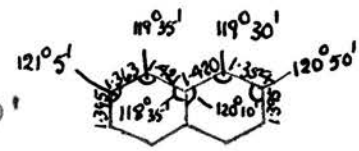
Whence $\sin\theta \doteq 1.42/2 \times 1.36$ from (1)

$$\therefore \theta \doteq 31.5^\circ$$

$$\therefore \theta - \phi \doteq +1.5^\circ.$$

Robertson et al. found differences of this order for $\theta - \phi$. Their full structure is shown below

$(\theta-\phi)_I = 2^\circ 10'$



$(\theta-\phi)_{II} = 45'$

$\therefore (\theta-\phi)$ average $= 1.5^\circ$.

They concluded that the accuracy of the bond length measurements was well within the limit 0·01 Å and the accuracy of the bond angles within the limit 0·4°. They pointed out that there were differences between chemically identical bonds (1·363 and 1·354 Å) and it is apparent that there are differences between chemically identical bond angles (118°35' and 120°10') which are beyond their limits of error; but Robertson et al. stressed that what are chemically identical are not necessarily crystallographically identical as the environment of the bonds and angles may differ in the cyystal. However stress should have been laid on the fact that a necessary corollary of the bond length differences is the occurrence of bond angle differences from 120°.

Anthracene. By a similar process

$$a + 2b \sin\phi = d + 2c \sin\theta \qquad \ldots (1)$$

Now Robertson, Sinclair and Mathieson (Acta Crystallographica, 1950, 255) have shown that $a = 1{\cdot}44$ Å, $b = 1{\cdot}42$ Å, $c = 1{\cdot}36$ Å and $d = 1{\cdot}39$ Å, i.e. $a > b > d > c$.

From (1) as $a > d$ $\quad 2b \sin\phi > 2c \sin\theta$

$$\therefore \frac{\sin\theta}{\sin\phi} > \frac{b}{c} \text{ and as } b > c$$

$$\frac{\sin\theta}{\sin\phi} > 1 \quad \therefore \theta > \phi$$

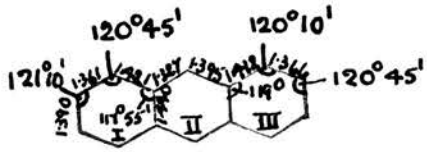
As before an approximate value for $\theta - \phi$ may be obtained from (1) by assuming $\phi = 30^\circ$ and giving a, b, c and d the values indicated above

$$1{\cdot}44 + 1{\cdot}42 \simeq 1{\cdot}39 + 2 \times 1{\cdot}36 \sin\theta$$

$$\therefore \sin\theta \simeq 1{\cdot}47/2 \times 1{\cdot}36 \qquad \therefore \theta \simeq 32{\cdot}75^\circ$$

$$\therefore \theta - \phi \simeq 2{\cdot}75^\circ.$$

The complete structure established by Robertson et al. is



$(\theta-\phi)_I \simeq 3^\circ 15'$ $\qquad$ $(\theta-\phi)_{III} \simeq 1^\circ 45'$. $\therefore (\theta-\phi)$ average $= 2{\cdot}5^\circ$

The same remarks may be made as for naphthalene above.

<u>Phenanthrene</u>. The argument for ring I is similar to those above for ring II.

$$e + 2a\sin\beta = f + 2e \times \sin\alpha.$$

If $\beta = \alpha = 30^\circ$. Then $e + a = f + e \quad \therefore a = f$

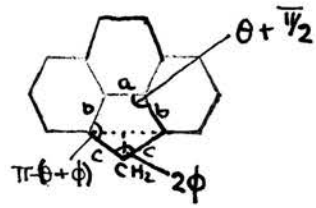
Now 'f' is certainly very much less than 'a'

Hence $\alpha \neq \beta \neq 30^\circ$ and the bond angles cannot be 120°.

As above an approximate value for the difference in the bond angles $(\pi/2 + \theta)$ and $(\pi/2 + \phi)$ may be obtained.

Differences in bond angles of this order have been found by Robertson et al. (loc.cit.) in the cases of naphthalene and anthracene but emphasis has been placed by them on the differences in bond length because the errors in the determination of bond length are not comparable to the differences in bond lengths whereas the errors in bond angles are comparable to the differences in bond angles; they should, however, have stressed that as a vital corollary to their demonstration of the bond length variation, bond angle variation must exist, although accurate values cannot yet be given to the angles. It is now suggested that differences in bond angles in six-membered rings may arise from a different cause, namely the differing stereochemical requirements of a ring with which it is condensed.

Phenanthrindene



If the bond lengths and internal angles of the five-membered ring of phenanthrindene be represented by the symbols shown in the above diagram, then

$$a + 2b \sin\theta = 2c \sin\phi \qquad \ldots (1)$$

If the internal angles $(\pi/2 + \theta) = 120^\circ$ then $\theta = 30^\circ$

$$\therefore \frac{a+b}{2c} = \sin\phi$$

By giving 'c' the value 1·54 Å (the value for the normal single bond) and 'a' and 'b' the values 1·42 Å (a fairly reasonable average value for such bonds in a polycyclic hydrocarbon) an approximate value for may be obtained

$$\sin\phi \simeq \frac{1{\cdot}42}{1{\cdot}54} \text{ in which case } \phi \simeq 67^\circ$$

The internal angles would then be

$$\left.\begin{aligned} (\pi/2 + \theta) &= 120^\circ \\ 2\phi &= 134^\circ \\ \text{and } (\pi - (\theta+\phi)) &= 83^\circ \end{aligned}\right\} \ldots \text{A}$$

These values seem ridiculous and the only solution is to alter θ to a reasonable value. If $\theta = 20^\circ$, i.e. $(\pi/2 + \theta) = 110^\circ$ then from the equation (1) giving 'a', 'b' and 'c' the values indicated

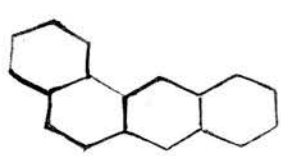
$$\sin\phi = \frac{1.42 + 2.84 \times 0.342}{3.08} \text{ ie. } \phi = 52^\circ$$

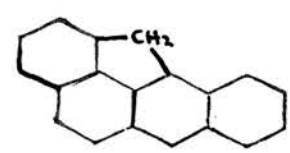
The internal angles would then be

$$\left.\begin{aligned} (\pi/2 + \theta) &= 110^\circ \\ 2\phi &= 104^\circ \\ \text{and } \pi - (\theta+\phi) &= 108^\circ \end{aligned}\right\} \ldots \text{B}$$

These values (B) are much more reasonable for a normal five-membered ring; it seems irrational to alter radically the values of the internal angles of a five-membered ring from their natural values so that the angles of the six-membered rings with which it is condensed may remain at or very close to 120°. It seems much more likely that the angles of the whole condensed system will absorb the "strain" which, in the previous approaches, has all been associated with the five-membered ring. In the case of phenanthrindene it seems certain that the angles external to the five-membered ring but internal to the six-membered rings are larger than 120° <u>if the molecule is planar</u>.

Now the question has been resolved into establishing the planarity of phenanthrindene. The first piece of evidence is the compatability of the spectra of phenanthrene and phenanthrindene which R.N. Jones (loc. cit.) claims to exist and the known similarity between the spectra of 1:2 benzanthracene and the methylene benzanthracene (1:2 benzphenanthrindene) (R.N. Jones).

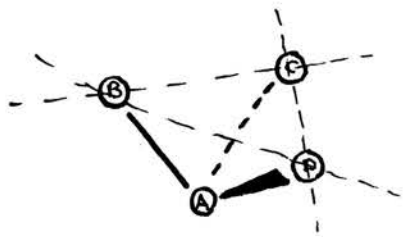




It may be argued that where the distribution of atoms within a plane is different from that in the comparison planar compound, a marked difference in absorption would exist just as would exist when comparing with a compound of a non-planar structure. Against this it may be said that where a planar structure exists, there is a plane about which the orbitals of the electrons involved in the absorption are symmetrically distributed, and so, when two planar compounds are being compared, a closer similarity in absorption spectra would be expected than when a planar compound and a compound of non-planar structure in which the plane of maximum density of atoms is not one of symmetry for the electron orbitals, are compared. The displacements of atoms within the plane would cause a first order effect on the absorption whereas a displacement out of the plane would cause a much more marked second order effect. Such a first order effect exists as R.N. Jones had described an increase in "F.s. Effect", i.e. the fine-structure, when condensed five-membered rings are present in many compounds such as the methylene benzanthracene above. This has been emphasized in earlier sections of this thesis in the case of very simple compounds, e.g. hydrindene, acenaphthene and fluorene.

The remaining evidence for the planarity of

phenanthrindene is its evident chemical similarity to phenanthrene; although some differences exist, they are no greater than would be expected when the differences between naphthalene and acenaphthene, and -xylene and hydrindene are recalled. Any marked deviation from planarity would probably cause significant differences in chemical properties. In the diagram below A is a carbon atom, in an aromatic hydrocarbon, joined to three other atoms which are not coplanar with it.

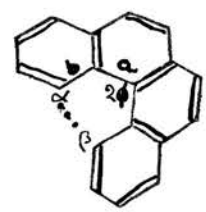


B, C and D may all be other nuclear carbon atoms or one may be an atom belonging to some peripheral group, e.g. a hydrogen atom. It is impossible, in this case, that a plane through A parallel to the plane containing B, C and D will be a plane of symmetry for the electron orbitals surrounding A. The electron distribution at A will be such that chemical attack from a particular direction will be favoured and compared with a planar compound in which the distribution at A will favour attack from two directions equally the non-planar structure will be more reactive.

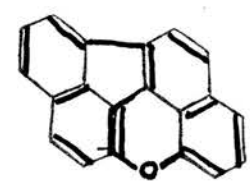
Until more coherent and reliable evidence is produced, it seems reasonable to take the planar structure of phenanthrindene as the more probable and it is therefore permissible to accept tentatively the suggestion of bond angle variation as a subject of argument. If this principle is then applied to the remainder of the fluorene series it is apparent that if the coronene-like compound I was synthesised or the compound II and if their physical properties, especially the X-ray diffraction of their crystals, were favourable to a planar structure, then the conclusion would be proved. Although I and II are unknown schemes for their synthesis, e.g. from phenanthrindene by the methods used to synthesise fluoranthene from fluorene, could be readily conceived.

I.

II.



III.



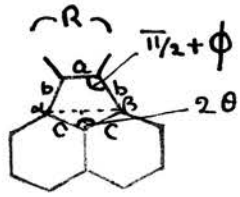
IV.

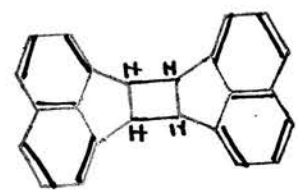
Comparison of II with the corresponding benzphenanthrene III is illuminating. The distance

$\alpha\beta = 2b \sin\phi$. If $\phi = 60^\circ$ and b is $\simeq$ 1·42 Å, $\alpha\beta$ = 2·46 Å. This gives some idea of the "distortion" required to bridge the gap. The possibility of synthesis of II and I may be questioned but a promising pointer exists in that a hetero-analogue of a benzo derivative of II is claimed to exist, IV. (Zincke and Pack, Monatsh., 1949, 80, 213-9).

Before considering fluorene itself it is of interest to examine acenaphthene, acenaphthylene, fluoranthene, heptacyclene and dihydrophenanthrene.

Acenaphthene, acenaphthylene, fluoranthene and heptacyclene





HEPTACYCLENE.

From this diagram it is apparent that $\alpha:\beta = 2c \sin$

If $\theta = 60^\circ$ and c = 1·42 then $\alpha\beta$ = 2·46 Å.

Now $\alpha\beta = a + 2b \sin\phi$

$\therefore \sin\phi = \frac{2.46 - a}{2b}$ if $2\theta = 120^\circ$.

In the case of acenaphthene a $\simeq$ 1·54 Å and b $\simeq$ 1·52 Å

$$\therefore \sin \phi = \frac{0.92}{3.04} \qquad \therefore \phi = 17.5^\circ.$$

In the case of acenaphthylene a $\simeq$ 1·34 Å and b $\simeq$ 1·50 Å

$$\therefore \sin \phi = \frac{1.12}{3.0} \qquad \therefore \phi = 22^\circ.$$

In the case of fluoranthene a $\simeq$ 1·40 Å and b $\simeq$ 1·44 Å

$$\therefore \sin \phi = \frac{1.06}{2.88} \qquad \therefore \phi = 21.5^\circ.$$

In the case of heptacyclene $\phi \simeq 17.5^\circ$ as the dimensions are similar to acenaphthene.

The internal angles of the five-membered rings would in these cases have the values indicated in the table below. Δ represents the deviation from the normal angles of a five-membered ring.

COMPOUND	2θ ANGLE ASSUMED	Δ	$\pi/2+\theta$	Δ	REMAINING $\angle$	Δ
Acenaphthene	120	+ 12	107·5	-0·5	102·5	-5·5
Heptacyclene	120	+ 12	107·5	-0·5	102·5	-5·5
Acenaphthylene	120	+ 12	112	+4	98	-10
Fluoranthene	120	+ 12	111·5	+3·5	98·5	-9·5

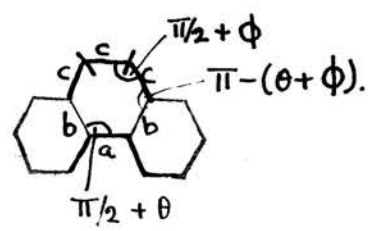
It is apparent from this analysis that the angle (assumed to be 120°) should be to some extent reduced, in

which case the contiguous internal angles of the naphthalenic moiety must be increased and corresponding changes be made in the other angles to give an acceptable model. It should be noted that an X-ray analysis of one heptacyclene, has been carried out and reported in note-form (Dunitz and Weissmann, Acta Crystall., 1949, 63). Two comments relevant to the above argument are quoted:

"The four-membered ring is one plane and the acenaphthylene parts are in planes at 45° to this. The sides of the 4-membered ring appear to be somewhat longer than 1·54 Å but accurate values are not yet available."

"Certain distortions from regularity also appear to exist in the naphthylene group."

Dihydrophenanthrene



By a similar analysis to that used previously

$$a + 2b \sin\theta = c + 2c \sin\phi$$

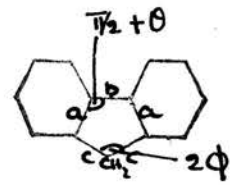
Now $a \doteq 1{\cdot}48$ Å, $b \doteq 1{\cdot}40$ Å, $c \doteq 1{\cdot}54$ Å,

and if $\theta = 30°$, i.e. $\pi/2 + \theta = 120°$.

Then $\sin\phi = \frac{1.48 + 1.40 - 1.54}{3.08}$ $\therefore \phi = 26^\circ$.

$\therefore$ The angle subtended by the methylene groups are 116° if $\pi/2 + \theta = 120^\circ$ and the values given to the bond lengths are justified. The remaining internal angles are then 124° and so it appears that there is/even in this case, some departure from the normally accepted values.

Fluorene



By applying the analytical procedure previously employed

$$b + 2a\sin\theta = 2c\sin\phi$$

If $\theta = 30^\circ$, i.e. $\pi/2 + \theta = 120^\circ$ and if $b \simeq 1.48$ Å, $a \simeq 1.40$ Å and $c \simeq 1.52$ Å

Then $\sin\phi \simeq \frac{1.48 + 1.40}{3.04}$ $\therefore \phi \simeq 71^\circ$.

Whence the internal angles are

$$\left.\begin{aligned} \pi/2 + \theta &= 120^\circ \\ 2\phi &= 142^\circ \\ \pi - (\theta + \phi) &= 79^\circ \end{aligned}\right\}$$

It was the difficulty of reconciling such values, required by a planar structure retaining a biphenyl-like nucleus, with accepted bond angle values that prompted the postulation of a non-planar structure.

At this stage it should be emphasised that a comparison of the absorption spectra of dibenzocycloheptadiene, dihydrophenanthrene and fluorene would be illuminating for dibenzocycloheptadiene is the first member of the polymethylene biphenyl series in which no strain due to the alicyclic ring would be absorbed by the whole system. Remembering Askew's curves for the absorption spectra for dihydrophenanthrene and fluorene the question arises would the strong serrations which are present in the fluorene curve and which are weakly mirrored in the dihydrophenanthrene curve have no equivalent in the dibenzocycloheptadiene curve (cf. Merkel and Wiegand, Zeit. für Naturforschung, 1948, Band 3b, Heft 3/4, 93). In the case of biphenylene where the four-membered ring would be expected to have an even higher effect the absorption curve is highly serrated (Carr Pickett and Voris, J.A.C.S., 1941, 63 3231-2).

The most significant evidence regarding the structure of fluorene comes from dipole moment studies. Hughes Le Fèvre and Le Fèvre (J., 1937, 202) have shown that the dipole moments of 2, 7-disubstituted fluorenes

differed from that of fluorene itself. In examining their results they made two important assumptions:

(1) The angles of the 5-membered ring are 108°,

(2) The angles of the 6-membered rings are 120°.

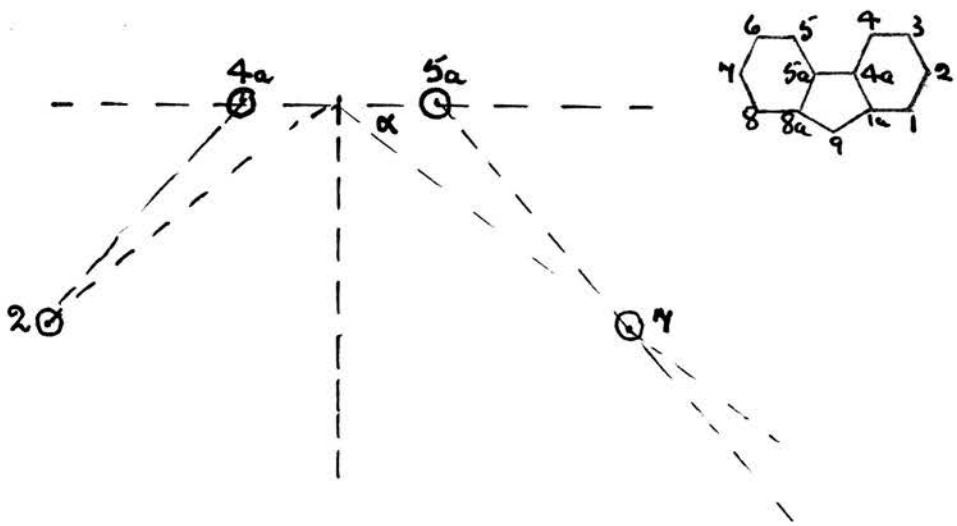
They then showed that the dipole moments were in agreement with a structure in which the six-membered rings had been displaced within the plane through an angle of 12°.

In an attempt to reach some conclusion regarding Cook and Iball's suggestion of non-planarity they examined their results on a model in which the planes of the six-membered rings could be inclined to the plane of the five-membered ring both from the point of view of cis- and trans-structures. Examination of the results for a series of compounds showed that no one form could be considered as suggesting a spatial structure typical of the series.

Their work is of fundamental importance but the interpretation of the results must be based on a model and the preconceptions of structure which are used in selecting the assumptions on which the models are based, must be examined. It is apparent that on their model, to retain the angles of the five-membered rings and of the six-membered rings intact, they postulated external angles of the order of 132°. This is possible, but it is more reasonable to assume that this value may be

reduced by slight alterations in the internal angles associated with them.

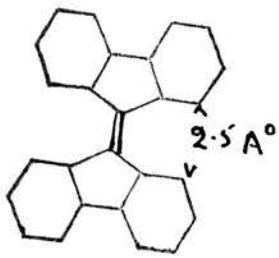
The most general conclusion that can be reached is that in the 2;7-disubstituted fluorene series, the components of the resolved molecular dipole, which may be associated with the individual substituent groups, are not collinear. If, as a first approximation, the direction of the substituent dipoles is considered to be along the line joining carbon atoms 2 and 4a and carbon atoms 7 and 5a then it may be concluded that atoms 2, 4a, 7 and 5a are not collinear, and taking a line through 4a and 5a as a reference it may be said that carbon atoms 2 and 7 are displaced from this line by an angle 'α' with reference to a point midway between 4a and 5a.

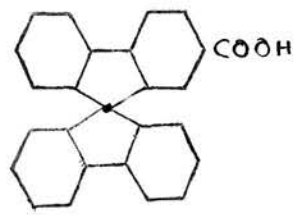


Nothing more may be said about the other atoms. The model that is suggested for fluorene is after this fashion and may be described as follows. The symmetry of fluorene about a line joining carbon atom 9 and the centre of a line joining carbon atoms 4a and 5a is apparent. About this line and in a plane containing it, the various carbon atoms are distributed in such a way that they absorb any strain imposed by a five-membered ring possibly by alterations in both bond lengths and bond angles. The stability of the compound and its close relationships with compounds which lack such an element of strain, indicate the equitable and ready distribution of the strain.

Cook and Iball re-examined the crystallographic data of Hengstenberg and Mark (Z. Krist, 1929, 70, 283) and decided that it supported a non-planar structure. It is significant that Stuart who had previously interpreted the results, preferred a planar structure and this lack of unanimity combined with a realisation of the technical difficulties which faced them at that period and which J.M. Robertson has only recently overcome, emphasise the care with which their work should be approached. Recently Fenimore (Acta Crystallographica, 1948, 295) has examined the structure of bis-biphenylene ethylene by X-ray methods.

He concluded that this compound had a planar structure and if his results are reliable this





bis-biphenylene ethylene

2-carboxy-9:9'spiro-difluorene

reflects on the structure of fluorene itself.

The chemical evidence is confused and the overall impression is that all claims to obtain isomeric 9-substituted fluorenes have on re-investigation proved to be spurious. They are reviewed by Cook and Iball who do not postulate isomers on a basis of their non-planar structure but suggest that "it may be that the molecule possesses sufficient elasticity to undergo oscillation between two non-planar forms". This can be restated as the energy barrier between the energy states corresponding to the cis- and trans-forms is not high, i.e. the planar form which must presumably be an intermediate in the change, no matter how transitory, has an energy state not

greatly different from that of either the cis or the trans. This is contrary to their initial supposition of strain in the planar structure. In addition it should be realized that the stabilising resonance energy must be greater in the planar than in either of the other forms. Weisburger and Ray (J.A.C.S., 1950, 72, 4 250) attempted to resolve 2-carboxy-9,9'-spirodifluorene and interpreted their failure to do so as evidence that fluorene is planar.

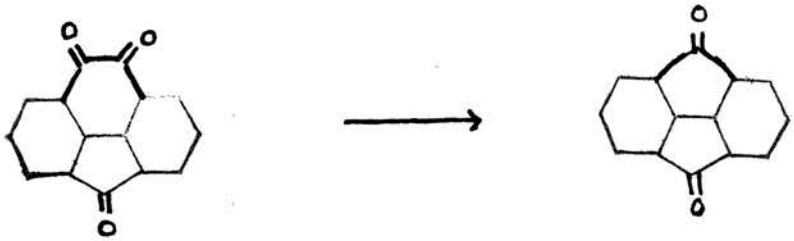
The question now rises as to how to prove or disprove this question of planarity. The first obvious answer is an exact X-ray analysis with modern refinements. In addition to the study of fluorene itself, the study of 2:7-dichlorofluorene would probably give a better solution to the problem, for the distance between the two chlorine atoms must be significantly different in the molecular models which are of planar structure or of cis or trans non-planar structures.

The dipole moment of fluorene itself which was quite large, should now be commented on. It is known that phenyl groups have a certain dipole moment and in the case of fluorene these come into operation by virtue of the effective displacement of the two phenyl groups of the biphenyl structure from the common line of symmetry. It is this dipole moment which probably causes the large diffusion current in the polarographic reduction of

fluorene (p. 19) compared with dihydrophenanthrene which probably has a smaller dipole moment.

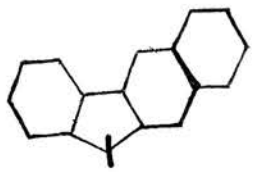
Mills, Parker and Tomkinson (J. 1924, 125, 2365) pointed out that fluorenone-4-carboxylic acid does not cyclise to 4:5-ketofluorenone. They advanced this as evidence of a non-planar formula. Rieveschl and Ray interpret this as evidence that "the bond joining the benzene rings is bent, increasing the distance between the 4 and 5 positions, which is to be expected if the compound has a planar formula." If what they meant by bent was that the electron orbitals involved in the union of atoms 4a and 5a are not symmetrically distributed about a plane through atoms 4a and 5a and perpendicular to the plane of the molecule, then they are correct. This distortion of the orbitals must arise whenever the external angles are enlarged to such an extent but whether the 'bending' of the bond and the greater distance between carbon atoms 4 and 5 are interrelated by more than that they are caused by the same process, namely the cyclisation that produces the five-membered ring, is doubtful. The problem is akin to the synthesis of phenanthrindone from phenanthrene 4-carboxylic acid. Whether this has been attempted is not known but it is unlikely to succeed for the same reason, namely the lack of the "flexibility" which permits the reaction process to occur. It is akin to the

comparative difficulty of cyclising 1-naphthylacetic acid to acenaphthenone and the comparative ease of cyclising 1-(1:2:3:4-tetrahydronaphthyl)-acetic acid to 1a: 1: 2: 3-tetrahydro-7-acenaphthenone (Johnson and Glen, J.A.C.S, 1949, 71, 1092). A much more fruitful procedure for the synthesis of 4:5-ketofluorenone would be by the Schmidt and Bauer ring contraction method on 4:5-ketophenanthraquinone.



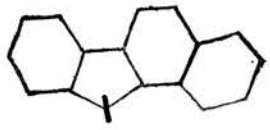
If formed and proved planar it would go far to demonstrate the certainty of variation in angle size.

Recently Orchin and Friedel (J.A.C.S., 1949, 71, 3002) pointed out that 1:2-benzfluorene, I, and 2:3-benzfluorene, II, are very similar in properties (absorption spectra, melting point and formation of complexes) whereas 3:4-benzfluorene III, and I and II are dissimilar in properties.

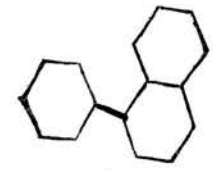


I.

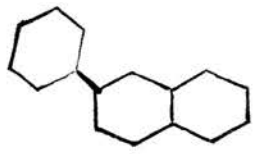
III.



II.



V.

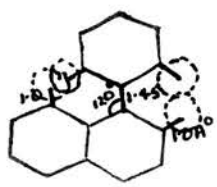


IV.

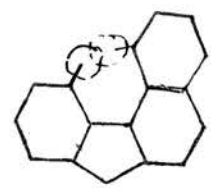
They contrasted the difference in properties with the difference between 2-phenyl naphthalene, IV, and 1-phenyl naphthalene, V. They discovered that the difference in absorption spectra between (I and II), and III was paralleled, by the difference between those of IV and V.

COMPOUND	M.P.	STABILITY OF COMPLEXES
I	186°C	+ [2:1]
II	214	+ [2:1]
IV	103	+ [2:1]
III	127°C	+++ [1:1]
V	45°C	-

They interpreted the low melting point of V and its failure to form complexes as being due to the steric inhibition of planarity by the hydrogen atoms at the and 8 positions. This conclusion was reached on the basis of a model represented by A.



A



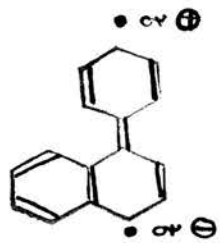
B

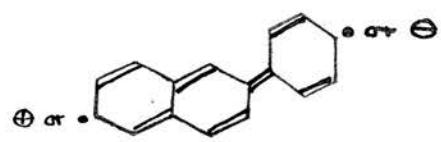
The fact that III and 1-phenyl naphthalene are similar in having lower melting points and having absorption spectra differing from (I and II), and IV respectively led them to conclude that, because a planar structure for III involved only a minor overlap of hydrogen atoms, a non-planar structure involving considerable overlap was probable (B). Their arguments and conclusions are open to two serious criticisms.

(1) <u>The planarity of 1-phenyl-naphthalene</u>. In this paper and an earlier one (Friedel, Orchin and Reggel, J.A.C.S., 1948, <u>70</u>, 199) make the tacit assumption that

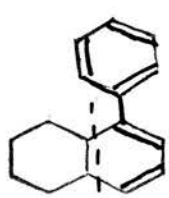
1-phenyl naphthalene and 2-phenyl napthalene should have closely similar spectra. This is improbable because there is interaction between the benzenoid and naphthalenoid rings - probably through the contribution of dipolar and diradical structures and these ~~dipolar~~ structures are different in the two cases

e.g.

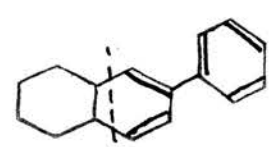




The problem is also akin to the influence of a phenyl group on the absorption in 2-phenyl butadiene and 1-phenyl butadiene.



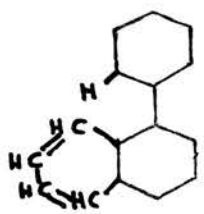
Extended Conjugation.



Partial Crossed Conjugation.

They base their arguments regarding the spectra of the 1- and 2-phenyl naphthalenes on the work of O'Shaughnessy and Rhodebush (J.A.C.S., 1940, 62, 2908)

on 2:2' disubstituted biphenyls and Pestemer and Mayer-Pitsch (Monatsh., 1937, 70, 104) on 2 mono-substituted biphenyls. They themselves showed that 2-methyl-biphenyl absorbs at shorter wavelengths and with lower $Log_{10}\varepsilon$ max. than biphenyl which is good evidence for interference between the methyl group and the 2' hydrogen atom. However in the case of the 2-amino and 2-nitro-biphenyls, Pestemer and Mayer-Pitsch found that their spectra were intermediate in position between those of the 3-(META-) and 4-(PARA-)substituted biphenyls which is expected OF AN ORTHO COMPOUND. Assuming that comparison of 2 and 1-phenyl naphthalenes is permissible then their evidence based on 2-methyl-biphenyl is very relevant for 1-phenyl naphthalene is in effect a 2-substituted biphenyl.



However the absorption spectra of 1-phenyl naphthalene, although more akin to that of naphthalene in shape has sufficiently different values for $\log_{10}\varepsilon$ max. to make the question remain in doubt.

It has long been realised that hydrogen atoms can be packed into surprisingly small spaces, e.g. Fenimore showed thattwo hydrogen atoms in the 1:1' positions of bisbiphenylene ethylene only took up 2·5 Å and it is therefore likely that in the case of 1-phenyl napthalene no serious constraint arises. Adams and Cairns (J.A.C.S., 1939, 61, 2179) have stressed that the stability of optically active 2-mono-substituted biphenyls is less than atomic radii calculations would indicate and as evidence there is the attempted resolution of 2 substituted biphenyls by Lesslie and Turner (J., 1933, 1589) which only succeeded in the case of 3'-bromo-2-biphenyl trimethylarsonium-iodide when even the 3'bromo-2-biphenyl trimethylammonium iodide had been unsuccessfully examined.

(2) Inconsistencies in their evidence. Several inconsistencies exist in their evidence, even in the comparison of absorption spectra. Their conclusion based on one range of spectra can be contradicted by selecting other ranges. See table below.

COMPOUND	λ MAX		LOG ε MAX		λ MAX		LOG ε MAX	
I	2620	Decreasing	4·95	Decreasing	3420	Decreasing	3·1	Increasing
II	2620		4·8		3390		3·9	
III	2320		4·7		3350		4·2	

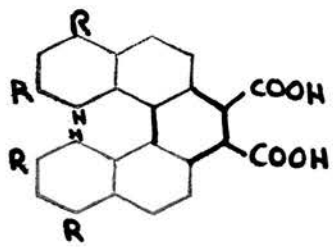
If planarity is inhibited in the case of III not only should its λ max values be less but the corresponding log ε max values should also be less than those of I and II. This is apparently untrue in the second maximum quoted.

In addition to this they use, as an important criterion for the similarity of I, II and IV, the stability and constitution of complexes. In the case of III and V, they do not explain why III forms extremely stable complexes whereas V does not form complexes at all.

It is apparent from this that their conclusions regarding the planarity of 3:9-benzfluorene and fluorene itself must be treated with considerable reserve especially as they are based on the extrapolation of questionable conclusions regarding 1-phenyl naphthalene to the fluorene series.

Recently Bell and Waring (J., 1949, 2690) have claimed some resolution of derivatives of 3:4:5:6 dibenzphenanthrene-9:10-dicarboxylic acid which have been interpreted on the basis of a non-planar structure for the dibenzphenanthrene nucleus. When the morphine salt

of 3:4:5:6-dibenzphenanthrene-9:10-dicarboxylic acid (R = H) was recrystallised evidence of rapid mutarotation was found. When the tetramethyl compound (R = CH_3) was used partial resolution was effected.

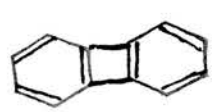


Whether this is evidence of the possibility of hydrogen atom interaction as claimed by Orchin and Friedel is questionable as the problem is much more acute in the above case.

The structure of fluorene has bean considered together with that of indene and cyclopentadiene by Pullman and Berthiers (Bull. soc., 1948, 551-4) and their electronic interpretations have proved to be disappointing. Although they could interpret the chemistry of cyclopentadiene on a basis of their calculations, they were less successful with indene and totally unsuccessful with fluorene. They concluded therefore that their models were incomplete.

The discussion of the fluorene series has enlarged the background in which the theory of resonance should be viewed. It has become apparent that it is now necessary to obtain a theoretical relationship between bond character and bond direction relative to other bonds linked to the same atom. This is likely to be important as it may serve to explain vital differences between benzene, azulene and cyclooctatetraene for if they are formulated on a planar basis, then the bond angles may be very important functions in determining the resonance interaction of the bonds and the inherent properties and stability of the system as a whole. It is now obvious that the six-membered ring is not a thing apart and it must be viewed in a new and enlarged perspective. Systems like that discussed based on cyclopentadiene should be considered for cyclobutadiene, cyclohexatriene, cycloheptatriene and cyclooctatetraene and members of these series do exist.

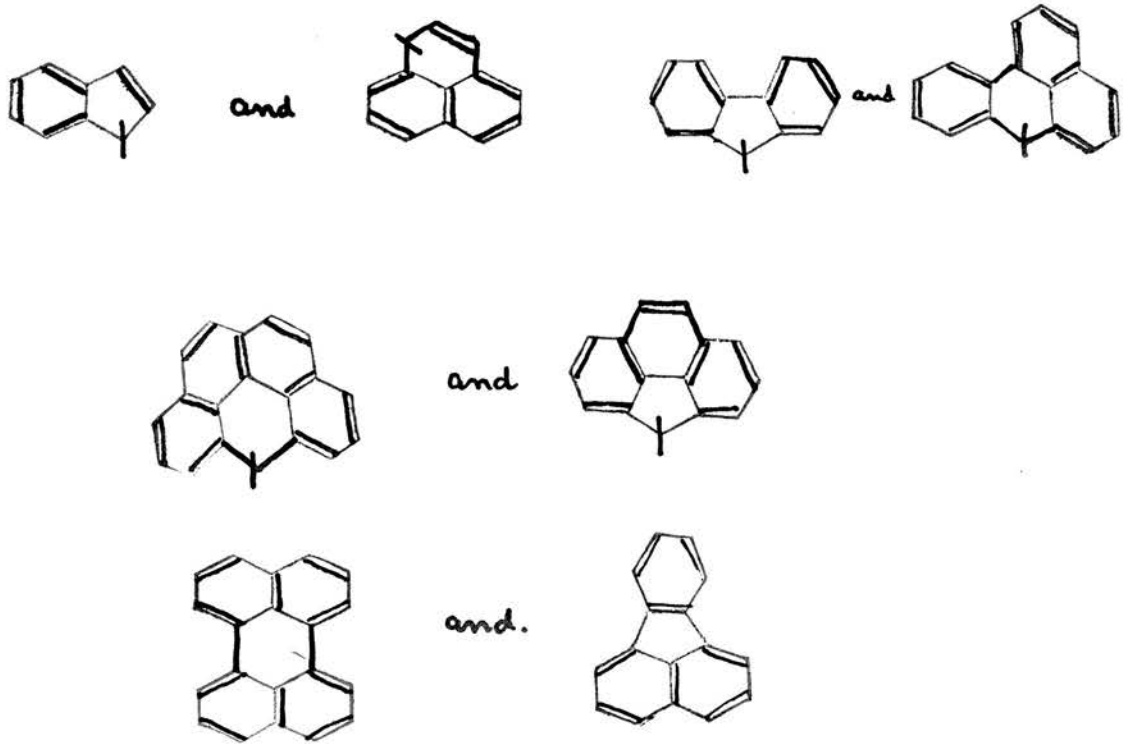
Cyclobutadiene. Debenzocyclobutadiene (biphenylene) is now available for study and should prove very interesting from the viewpoint of resonance energy, etc.



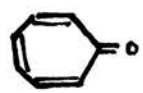
It is apparent that to give the internal angles their

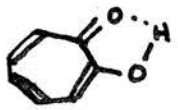
normal values would make the external angles very large. It would be of fundamental importance if this external angle should be found to be reduced in the actual structure. The reference to differences in reactivity due to bond angles, i.e. the unsymmetrical bond orbital distribution round an atom, may be recalled here for the ready hydrogenation of biphenylene to biphenyl (Baker, loc.cit.) must occur by virtue of an attack at a position where the bond angles are very varied (90, 120, 150°).

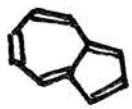
Cyclohexatriene. Compounds based on benzene may be listed together with their cyclopentadiene analogues, e.g.



Cyclohe$_{pt}$atriene. The recent syntheses of tropone and its derivatives (Dauben and Ringold, J.A.C.S., 1951, 73, 876, Doering and Detart, ibid, 877, Cook Raphael$_{Gibb}$and SOMERVILLE, J., 1951) and recent work on the azulenes and their derivatives have demonstrated the inherent stability of such structures.

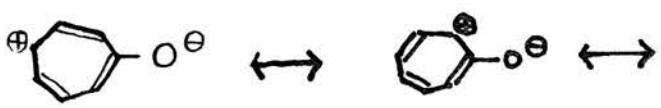






tropone tropolone azulene

In the case of tropone this may be represented by writing several canonical forms including such dipolar forms as



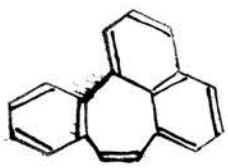
etc., etc.

If tropone is planar, as appears likely then its internal angles must be $5\pi/7$ i.e, 128·5°. Robertson has

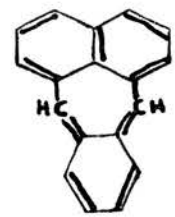
shown that Copper tropolone is planar and the resonance energy of tropolone has been found to be c. 28 K cals per mole and of tropone c. 21 K cals per mole. Hence the change in bond angle, although a reduction in resonance energy has occurred, has not completely erased the stabilising energy of this heptacyclic structure.

Condensed derivatives of tropene would be extremely interesting in so far as they would tend to reduce the neighbouring internal angles of the rings with which they were condensed

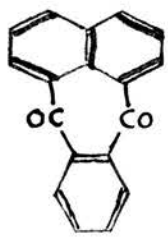
e.g.



and



The dihydro and diketo derivatives of the latter are known.



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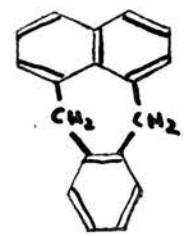


Cyclooctatetraene. The very marked differences in stability between cyclooctatetraene and benzene may well be due to the fact that if it is planar its internal angles would be $6\pi/8$ i.e. 135°. This value may be beyond the limit when resonance between neighbouring bonds may occur.

In the foregoing pages an attempt has been made to review critically some highly interesting problems concerning fluorene primarily but with a considerable relevance to a rapidly expanding field of organic chemistry. The views expressed are not to be regarded as in any way fixed but as a transitory stage which will suffer many changes as new evidence accumulates, before a satisfactory and complete explanation of the problems of aromatic structures is completed.

PART II

INTRODUCTION

In this part the material is presented in the form of several papers. Each paper is introduced with a summary and contains, where necessary, a review of the relevant literature.

Section I (i) The Attempted Synthesis of fluorene derivatives by the diene action.

(ii) Two enolbetaines of the hydrindene series.

Section II (i) The substitution reactions of 2-amino-fluorene.

(ii) The synthesis of fluorene-3-carboxylic acid.

Section III The Michael Condensation in the synthesis of fluorene derivatives.

PART II

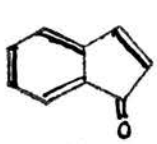
Section I (i)

"THE ATTEMPTED SYNTHESIS OF FLUORENE DERIVATIVES BY THE DIENE REACTION"

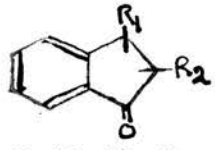
SUMMARY

The attempted synthesis of indone,I - a possible dienophile for the synthesis of fluorene derivatives by the diene reaction- by the dehydrohalogenation of 2-bromo-1-hydrindone,II, and 3-bromo-1-hydrindone,III, and by the hydrolysis of indone oxime has been unsuccessful. The synthesis of 1:2-dimethyl-1:2-dihydroxyhydrindene,IV, which is a possible precursor of 1:2 - dimethylenehydrindene,V,(cf. Campbell and Gow, J.,1949, 1555) is reported.

Fluorene derivatives have been synthesised by the action of dienes with indene followed by dehydrogenation

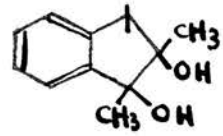


I.



II. R_1=H, R_2=Br.

III. R_1=Br, R_2=H.



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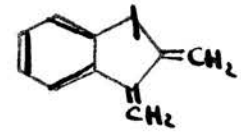


V.

(Swain and Todd, J.,1942, 626; Alder and Rickert,Ber.,1938, 71, 382).

Forcing conditions have usually to be used, but the replacement of indene by indone would be expected to facilitate the reaction and widen its scope. Three possible syntheses of indone have been investigated, none of which proved to be promising. They are

(1) the dehydrohalogenation of 2-bromo-1-hydrindone

(2) the dehydrohalogenation of 3-bromo-1-hydrindone

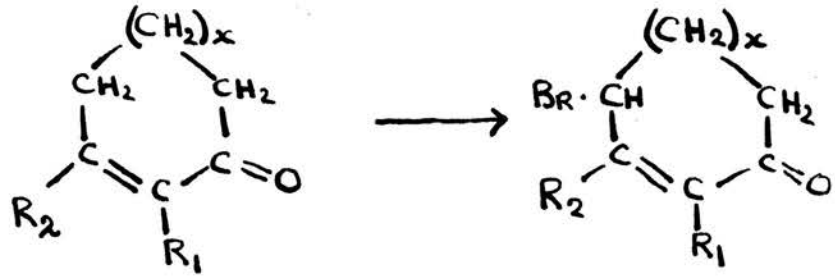
(3) the hydrolysis of indone oxime.

Many complex derivatives of indone are known (c f. Remo De Fazi, Gazz., 1924, 54, 996-1000; ibid., 1000-9) but few simple derivatives are reported. 2-methylindone has been prepared by the action of sulphuric acid on α-methylallocinnamic acid (Stoermer and Voht, Ann., 1915, 409, 55) and by treatment of 2-bromo-2-methyl-1-hydrindone with pyridine (Kizhner, Abs., 1934, 28, 1692). The physical constants given by these workers agree and both groups mention the instability of the compounds. Stoermer and Laage (Ber., 1917, 50, 981-9) prepared 3-methylindone by the action of concentrated sulphuric acid on β-methylallocinnamic acid but the compound (obtained in low yield) could only be isolated as a highly coloured oil suggesting that decomposition had occurred on distillation. Various halogenoindones have been prepared (Zincke, Ber., 1887, 20, 1269; Roser, Haselhoff, Ann., 1888, 247, 146; Schlossberg, Ber., 1900, 33, 2426) usually by

cyclisation of the corresponding allocinnamic acid by sulphuric acid or phosphorous pentoxide. Such a cyclisation procedure had been shown to give no indone but only truxone when allocinnamic acid itself was used (Liebermann, Ber., 1898, 31, 2095). It was decided that the method of Kizhner would be applied to 2-bromo-1-hydrindone in an attempt to prepare the parent substance indone.

2-bromo-1-hydrindone (Kipping, J., 1884, 500) when treated with pyridine gave only the pyridinium bromide and on prolonged heating small quantities of intractable oils which failed to give a ketonic reaction. Treatment of 1-hydrindone-2:N-pyridinium bromide with cold, dilute alkali gave the corresponding enolbetaine (see subsequent paper). Replacement of pyridine with triamylamine, triethylamine and dimethylaniline under a variety of conditions gave no evidence of indone formation.

3-bromo-1-hydrindone was prepared by reacting 1-hydrindone with N-bromosuccinimide in carbon tetrachloride. There was no evidence that 2-bromo-1-hydrindone was simultaneously formed and the formation of the 3-, in preference to the 2-isomer may be considered to be an extension of the discovery of Solway and Laforge (J.A.C.S., 1947, 69, 979) and Meystre and Wettstein (Experientia, 1946, 2, 408) that alicyclic α:β-unsaturated ketones react with N-bromosuccinimide in the allylic rather than α-methylenic position.



In the preparation hydrogen bromide was evolved, usually starting about 45 minutes after boiling was begun. Intermolecular dehydrohalogenation was apparently occurring. It was considered preferable to have no residual hydrindone and as a consequence boiling was continued even after this evolution was observed. The purification of the 3-bromo-1-hydrindone from the reaction mixture was found to be difficult and the low yield of pure compound (40-50%) is no reflection on the outcome of the principal reaction. The mother liquors from the recrystallisation of 3-bromo-1-hydrindone yielded its dinitrophenyl-hydrazone copiously although only an oil could be isolated on concentration. This difficulty of efficient isolation is the limit to the usefulness of this reaction.

The structure of the 3-bromo-1-hydrindone was shown by

(1) Differentiation from 2-bromo-1-hydrindone (Table I)

(2) Demonstrating the lability of the bromine to alkali

(3) Oxidation to phthalic acid (isolated as the anhydride) rather than to a bromophthalic acid.

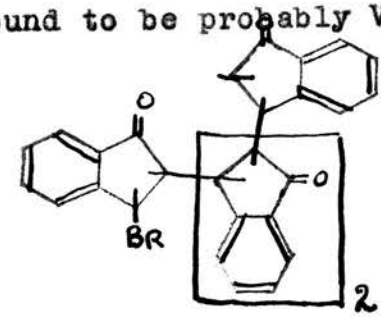
TABLE I

Compound	M.P.	M.P.D.N.P.	Description D.N.P.
3-bromo	57°C.	232°C.	Orange needles
2-bromo	39°C.	215°C.	Carmine needles

The attempted intramolecular dehydrohalogenation of 3-bromo-1-hydrindone was unsuccessful. The evidence indicates that intermolecular dehydrohalogenation is predominant. Treatment with various basic reagents gave mixtures from which no simple ketone could be isolated except occasionally a little unchanged 3-bromo-1-hydrindone.

Organic bases Pyridine, triethylamine and dimethylaniline gave mostly water soluble materials and intractable and non-ketonic oils.

Alumina Rapid filtration through a short column of alumina gave a mixture of white solids which could be separated by repeated fractional precipitation from benzene with petrol ether into four fractions. One of these, on analysis, was found to be probably VI



VI.

A whole series of related compounds seem to be formed. No indone is produced.

Sodium acetate On boiling 3-bromo-1-hydrindone with sodium acetate (anhydrous) in benzene for 30 minutes 80% of the bromine was found (gravimetric determination as AgBr) in the insoluble layer. The benzene layer was examined for indone and 3-acetoxy-1-hydrindone, neither of which was formed. The only products seemed to be high melting solids and intractable oils which gave no ketonic derivatives. In case indone was transitorily formed several moles (1→5) of dicyclohexenyl (Barnett and Laurence, J., 1935, 1104) were added to the benzene in several experiments before boiling, but no substituted tetrahydrofluorenone could be detected by chromatographic separation followed by attempted D.N.P. formation in the fractions.

The impression gained in this work was of the lability of the bromine in the 3-position. On standing in air or in the light it rapidly darkens with loss of HBr and soon becomes an oil. This is especially true of slightly impure samples. The low bromine analysis is probably explained by this decomposition. Throughout, the dehydrohalogenation seemed to occur intermolecularly.

Indone oxime has been described by Marckwald (Ber., 1895, 28, 1504) as a red viscous oil and was prepared from indene

by reaction with sodium ethoxide and an alkyl nitrite in ethanol. Repetition of this work followed by sublimation of the product in a high vacuum (by James Blair, Esq., B.Sc.) yielded indone oxime, M.P. 78°C., as yellow crystals. The yield was too poor to justify intensive hydrolytic studies.

In view of the success of Campbell and Gow's synthesis (loc. cit.) of fluoranthene derivatives by the simultaneous dehydration of trans-7:8-dimethyl-7:8-dihydroxyacenaphthene and diene reaction of the 7:8-dimethyleneacenaphthene resulting, with dienophiles, the analogous reaction of 1:2-dimethyl-1:2-dihydroxy-hydrindene was attempted with acetic anhydride as dehydrating agent and maleic anhydride and naphthoquinone as dienophiles. In neither case did the desired reaction occur. This was not unexpected. The synthesis of the glycol is reported in 50% yield (pure material) but the residual material was a mixture of ketones possibly containing 1:1-dimethyl-2-hydrindone and 2:2-dimethyl-1-hydrindone from pinacone transformation of the glycol or its stereo isomer which may have been formed.

The synthesis of ω -bromo-phthalide by reaction of phthalide with N-bromosuccinimide with carbon tetrachloride in presence of a peroxide catalyst is also recorded. This was an intermediate intended for the synthesis of 1-hydrindone-4-carboxylic acid. This work was discontinued.

EXPERIMENTAL

3-bromo-1-hydrindone. Hydrindone (1.32 gms., M.P. 41°C.) and N-bromosuccinimide (1.78 gms., M.P. 172°C., Ziegler et al., Ann., 1942, 551, 109) were added to carbon tetrachloride (15 mls.) which was boiled under reflux for 90 minutes. After cooling thoroughly succinimide (0.98 gms.) was removed by filtration. The combined filtrate and washings (total 25 mls. carbon tetrachloride) were concentrated to 10 mls. and diluted with petrol ether (20 mls., B.P. 40-60°C.). A further deposition of succinimide occurred. The filtrate was distilled under reduced pressure (20 mm. Hg) to remove solvent. The resulting yellow oil (1.98-2.05 gms) was triturated with petrol ether (B.P. 40-60°C.) containing 10% by volume of ethyl acetate. Eventually the oil became a mush of crystals which were removed by filtration, from the adhering oily particles and from the trituration liquor. The oil from the filtrate was retriturated until further treatment was abortive and no crystals separated. The combined solid (c.1 gm., M.P. 45-50°C.) was recrystallised from petrol ether / ethyl acetate, a little ethyl acetate or aqueous methanol. Rosettes of prisms were produced, seeding with the impure solid usually being required. The solid (0.8-9 gms., M.P. 52-3°C.) was recrystallised further

till its melting point was constant at 57°C.

C_9H_7OBr requires 38.1% Br.
Found 37.4% Br.

The dinitrophenylhydrazone formed orange needles (glacial acetic acid) M.P. 232°C. (subl.).

$C_{15}H_{11}BrN_4O_4$ requires 16.6% N.
Found 16.3% N.

2-bromo-1-hydrindone forms a dinitrophenylhydrazone crystallising from glacial acetic acid as carmine needles, M.P. 215°C.

$C_{15}H_{11}BrN_4O_4$ requires 20.4% Br.
Found 19.8% Br.

Oxidation of 3-bromo-1-hydrindone 3-bromo-1-hydrindone (70 mgs.) were boiled with caustic soda (3 mls. c IN.) and finely powdered potassium permanganate (100 mgs.). After 30 minutes sulphurous acid and sulphuric acid (2N) were added to acidify and decolourise the solution which was then thoroughly extracted with hot chloroform for 30 minutes. The chloroform layer was separated and dried (Na_2SO_4) and taken to dryness under reduced pressure. The residue (35 mgs.) obtained, was micro-sublimed and phthalic anhydride was obtained in the characteristic manner. Its melting point and mixed melting point confirmed its identity.

Dehydrohalogenation of 2-bromo-1-hydrindone Treatment of 2-bromo-1-hydrindone with pyridine under the conditions of Kizhner were ineffective. Substitution of pyridine by the bases indicated above under a variety of conditions of temperature, solvent and time, proved unavailing.

Dehydrohalogenation of 3-bromo-1-hydrindone 3-bromo-1-hydrindone (0.5 gms.) in benzene (2 mls.) were filtered rapidly through alumina (5 gms.). The material (0.2 gms.) removed by washing the alumina with 5% ethanol in benzene (20 mls.) was dissolved in hot benzene (3 mls.) and on addition of light petroleum (10 mls.) a white solid was deposited. This was separated and was again precipitated from benzene solution with light petroleum. Further fractional precipitation of this solid and of the material in the mother liquors yielded four solids of reasonably sharp melting-points. One of M.P. 292°C. was sent for carbon, hydrogen analysis and molecular weight determination. It then became apparent that not all the bromine had been removed and this was shown by an elements test.

$C_{36}H_{25}O_4Br$ requires	71.9% C.	4.3%H	M.W. 621.
Found	71.9% C.	4.2%H	M.W. 601.

Dehydrogenation in presence of dicyclohexenyl 3-bromo-1-hydrindone (1 gm.) in benzene (10 mls.) containing dicyclohexenyl (3 gms., M.P. 28°C.) was boiled with powdered sodium

acetate (2 gms. [fused]). After 30 minutes the suspended solid was removed by filtration and was taken up in 15% nitric acid (10 mls.) after drying. Excess silver nitrate solution (4%) was added and the precipitated silver bromide was filtered in a tared sintered funnel. After washing and drying by the standard procedures the silver bromide was weighed. 80% of the original quantity of bromine was present as silver bromide.

The benzene was concentrated to 5 mls and was chromatographed on alumina (50 gms.). No ketone could be shown by dinitrophenylhydrazone formation in any of the fractions.

Dicyclohexenyl The method of Barnett and Laurence gave poor results due to the age of the aluminium powder used in the bimolecular reduction of cyclohexanone. Replacement of the powder with small pieces of aluminium foil, made by rolling commercial aluminium sheet, and extension of the time of boiling to 6 hours gave almost double the quoted yields of 1:1'dihydroxydodecahydrobiphenyl. Their method, otherwise, gave excellent and reproducible results.

Indone oxime Amyl nitrite (11.7 gms.) in ethanol (25 mls.) were added dropwise to indene (11.6 gms.) in ethanol (100 mls.) containing dissolved sodium (2.3 gms.). The mixture was kept, during the addition, at 0-10°C. in an ice bath but the temperature was then allowed to rise to room temperature. After 24 hours, water (200 mls.) was added and the resulting solution

was extracted with ether (3 x 100 ml portions) which was discarded. Acidification of the aqueous layer with dilute hydrochloric acid gave an oil which was extracted into the ether (2 x 100 ml. portions). The oxime was re-extracted from the combined ether layers with caustic soda (100 ml 2N) and was again precipitated with acid and extracted into ether. The ether layer was separated and after drying over sodium sulphate was taken to dryness on the water-bath. The dark evil smelling oil (c 10 gms.) was subjected to hyvac. sublimation (60°C., 0.0001 mm. Hg) and a yellow solid sublimed. This was obtained in poor yield and after recrystallisation (methanol) melted at 78°C.

C_4H_7ON requires 74.5%C. and 4.8%H.

Found 74.0%C. and 4.8%H.

1:2 dimethyl-1:2-dihydroxyhydrindene Powdered 1:2 diketohydrindene (1.46 gms., M/100, Graham, Levin and Kolloff, J. Org. Chem., 1944, 9, 384; Perkin, Roberts and Robinson, J. 1912, 232) were added to a 100% excess of methyl magnesium iodide ($^M/_{25}$) in ether (50 mls.). A rapid reaction occurred with deposition of a Grignard complex. After one hour at room-temperature the mixture was decomposed with ice-cold ammonium chloride solution (10%) - external cooling being applied. A permanganate colour developed and was only dispelled after adding a considerable excess of ammonium

chloride solution. The ether layer was separated and the aqueous layer was extracted with hot chloroform for 2 hours. The combined extracts, ether and chloroform, were dried (Na_2SO_4) and concentrated at 30°C./20 mm. Hg. The residue was sublimed on the steam bath at atmospheric pressure. A white solid - the glycol - sublimed leaving a dark oil which gave a ketonic reaction. Yield 0.83 gms. M.P. 148-9°C. Recrystallisation from light petroleum gave a product M.P. 150°C. (slender white needles).

$C_{11}H_{14}O_2$ requires 74.1%C. 7.9%H.

Found 73.9%C. 7.9%H.

ω-bromo-phthalide Phthalide (1.34 gms.) in carbon tetrachloride (10 mls) were boiled with N-bromosuccinimide (1.78 gms.) and dibenzoylperoxide (10 mgs.). The solution became very dark. After 2 hours the solution was cooled to 0°C. and was filtered. The filtrate was warmed and diluted with 40 mls petrol ether (B.P. 40-60°C.). Crystals of ω-bromophthalide separated. The initial crop and a second crop from the concentrated mother liquors amounted to 2.05 gms., M.P. 86°C. (Lit 86°C.)

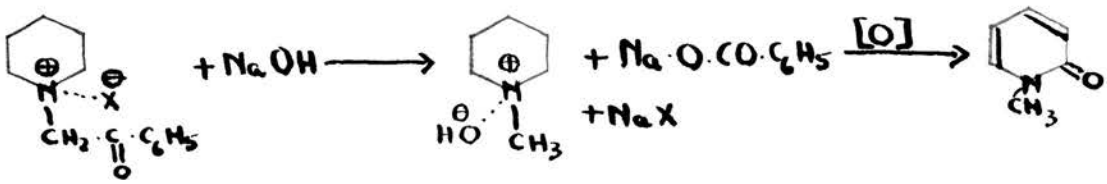
PART II

Section I (ii)

Two enolbetaines of the hydrindene series

Summary: The chemistry of the enolbetaines is reviewed. Two enolbetaines, 1-hydrindone-2N-pyridinium enolbetaine and 1:3-diketohydrindene-2N-pyridinium enolbetaine have been synthesized and some of their properties have been examined.

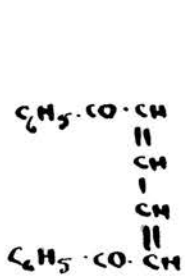
The enolbetaines. Bamberger (Ber., 1887, 20, 2344) discovered that treatment of phenacyl pyridinium bromide, I, with alkali yielded sodium benzoate. He was of the opinion that the phenacyl pyridinium bromide decomposed in the presence of alkali to give phenacyl bromide or phenacyl alcohol which reacted further to give benzoic acid. Since, however, Zincke (Ann., 1882, 216, 311) had shown that the action of alkali on phenacyl halides and phenacyl alcohol does not give benzoic acid, Bamberger's theory is untenable. Schmidt and van Ark (British Abs., 1900, i, 687) later showed that aqueous sodium carbonate reacted with phenacyl pyridinium bromide to give sodium benzoate and N-methyl pyridinium hydroxide, II. Later workers (Babcock and Fuson, J.A.C.S., 1933, 55, 2946) showed that the pyridinium compound produced was oxidised by alkaline ferricyanide to N-methyl-pyridone III, presumably through a pseudo-base.



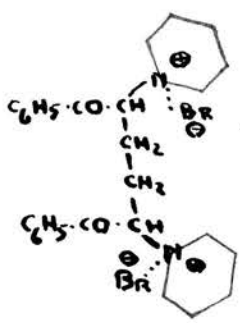
I II III

The generality of this reaction first became apparent when three groups of workers within one year reported independent observations on the "acid cleavage" of phenacyl pyridinium compounds.

(1) Babcock, Nakamura and Fuson (J.A.C.S., 1932, 54, 4407) while attempting to prepare 1:4-dibenzoylbutadiene, IV, by alkaline decomposition of 1:4-dibenzoyl-1:4-butane dipyridinium bromide, V, discovered that benzoic acid was the principal product. They then studied the reaction of phenacyl pyridinium bromide and p- bromophenacyl pyridinium bromide. Their work is shown schematically below.

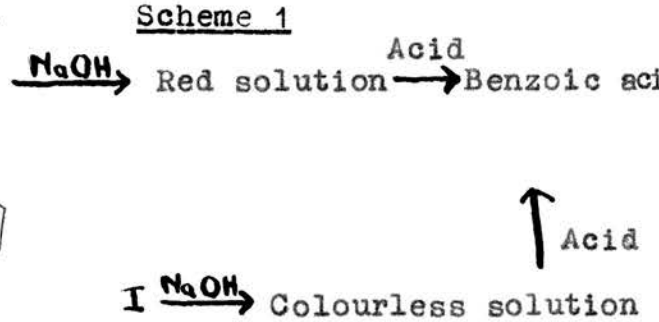


IV



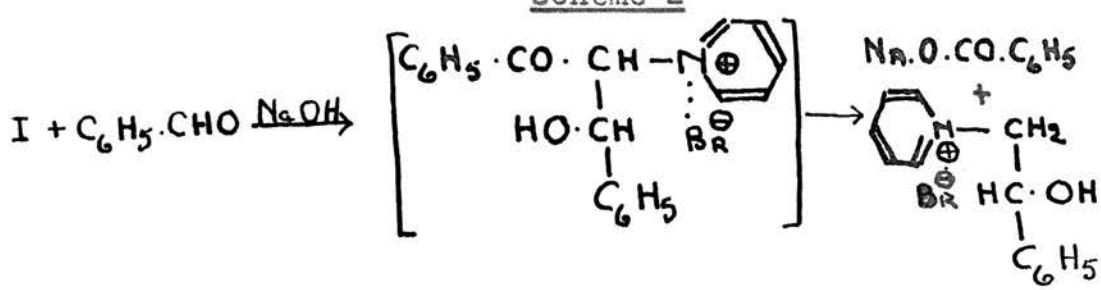
V

Scheme 1



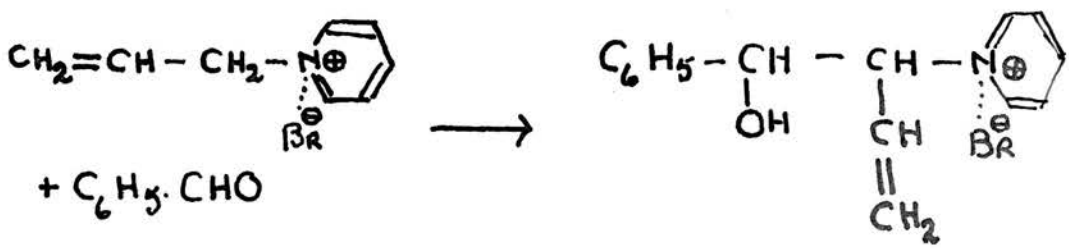
(2) Kröhnke (Ber., 1933, 66B, 604-10) discovered that the reaction of phenacyl pyridinium bromide with benzaldehyde in the presence of 1 mole. of alkali yielded the bromide of the pyridinium ethanol, VI. Subsequent investigations showed that the reaction pursued the course indicated below, Scheme 2 (Kröhnke and Fusold, Ber., 1934, 67B, 656-7; Kröhnke, Ber., 1935, 68B, 1351-9).

Scheme 2

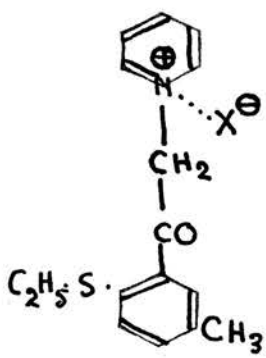


The essential feature of this reaction is that it is a typical reaction between an aldehyde and a compound containing a reactive methylene group. That a carbonyl group was unnecessary for this activation was proved by Kröhnke who showed that benzaldehyde reacted extremely readily with allyl pyridinium bromide (Scheme 3).

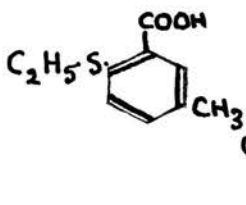
Scheme 3



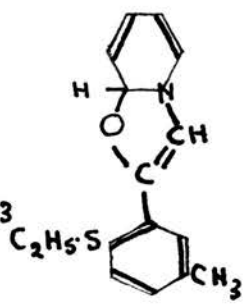
(3) Krollpfeiffer and Müller (Ber., 1933, 66B 739-43) reported that treatment of the pyridinium halides derived from O-(ω-haloacyl)-thiophenol ethers, VII, with alkali gave the corresponding ether of a thiosalicylic acid, VIII. As intermediates of this acid cleavage they isolated reactive crystalline compounds, orange in colour. No conclusion was reached regarding the structure of these compounds but the suggestion was made that the products were either anhydrobases, e.g. IX, or enolbetaines, e.g. X. (cf. Pfeiffer, Ann., 1928, 465, 20).



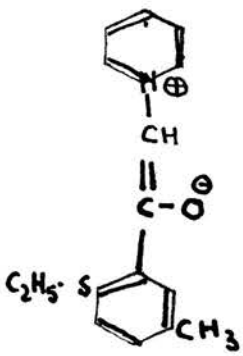
VII



VIII



IX

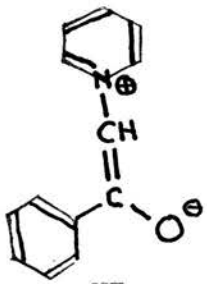


X

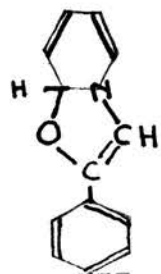
The isolation of these compounds by Krollpfeiffer and Müller initiated a considerable amount of work by Krollpfeiffer and Kröhnke on this type of compound.

The Structure of the Enolbetaines. Kröhnke (Ber., 1935, 68B, 1177-95) isolated the compound from phenacyl pyridinium bromide corresponding to the orange intermediate prepared by Krollpfeiffer in the phenacyl thio-ether series and established the mild conditions which made the isolation of

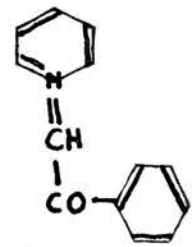
the alkali sensitive "intermediates" of the acid cleavage possible. The ease of regeneration of the phenacyl pyridinium halide by treatment of the intermediate with acid restricted the possible formulations to XI, XII and XIII.



XI



XII



XIII

Structure XII was incompatible with the high colour of the compound and XIII besides conflicting with the modern conceptions of the nitrogen atom would involve an evident similarity to the nitrenes which does not exist . The enolbetaine structure, XI, was left by elimination and agreed with the chemical and physical properties of the compound.

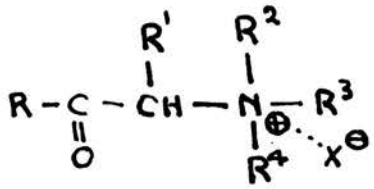
The requisite molecular specifications governing the existence of enolbetaines are the presence in the molecule of

(1) an enolisable group

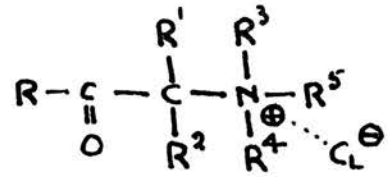
(2) a quaternary nitrogen atom.

Halides of structure XIV fulfil these conditions but structure XV does not as enolisation is impossible. As halides of structure XV do undergo acid cleavage (Krollpfeiffer and Müller, Ber., 1935, 68B, 1169-77) it is apparent that the enolbetaines are not essential intermediates in acid

cleavage although the enolbetaines do suffer acid cleavage.

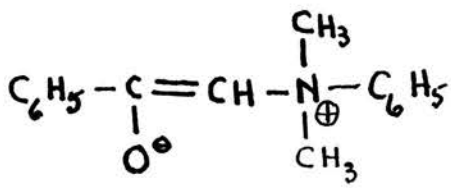


XIV

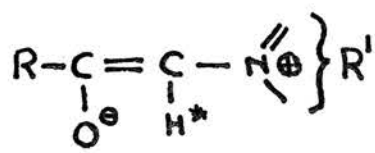


XV

In structure XIV, R and R' may vary widely and the properties of the resulting betaines are influenced to a considerable extent by the nature of the substituents. The quaternary nitrogen atom need not be contained in a heterocyclic aromatic compound since Kröhnke and Heffe (Ber., 1937, 70B, 1420-7) prepared the enolbetaine from phenacyldimethylphenyl ammonium chloride, XVI. This was colourless and differed considerably in properties from the corresponding pyridinium compound. This is discussed in the sections on colour and chemical properties.



XVI



XVII

Heterocyclic amines are the commonest compounds used in the preparations of betaines especially pyridine, quinoline, isoquinoline and the picolines. The derived betaines differ

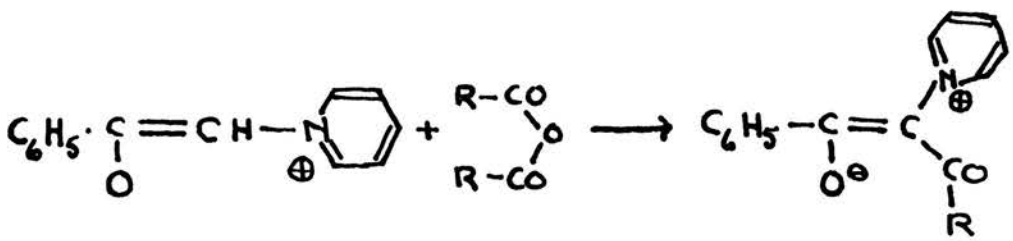
somewhat in depth of colour and in stability.

The properties of the Methine enolbetaines. Kröhnke and Kubler (Ber., 1937, 70B, 538) named enolbetaines of structure XVII methine enolbetaines, because of the reactivity of the methine hydrogen atom. The methine enolbetaines form hydrates which are generally yellow or orange in contrast to the anhydrous or less hydrated betaines which are orange or red. The most characteristic reaction of these compounds is the formation of complexes such as those with phenacyl pyridinium salts or more important those with picryl chloride and halogenoquinones such as chloranil (Kröhnke and Schmeiss, Ber., 1937, 70B, 1728-32). The latter are highly coloured and give coloured solutions at great dilution.

The compounds are low melting, few melting above 170° and most with decomposition. It is significant that their physical properties have not been intensively investigated and so in a later section (page 221) the examination of the absorption spectra of two enolbetaines - not however of the methine enolbetaine type - are recorded. The absorption spectra and dipole moments of these compounds would be of fundamental importance to the complete elucidation of structure in this series and a more intensive investigation should be initiated.

Their chemical reactions are typical of compounds

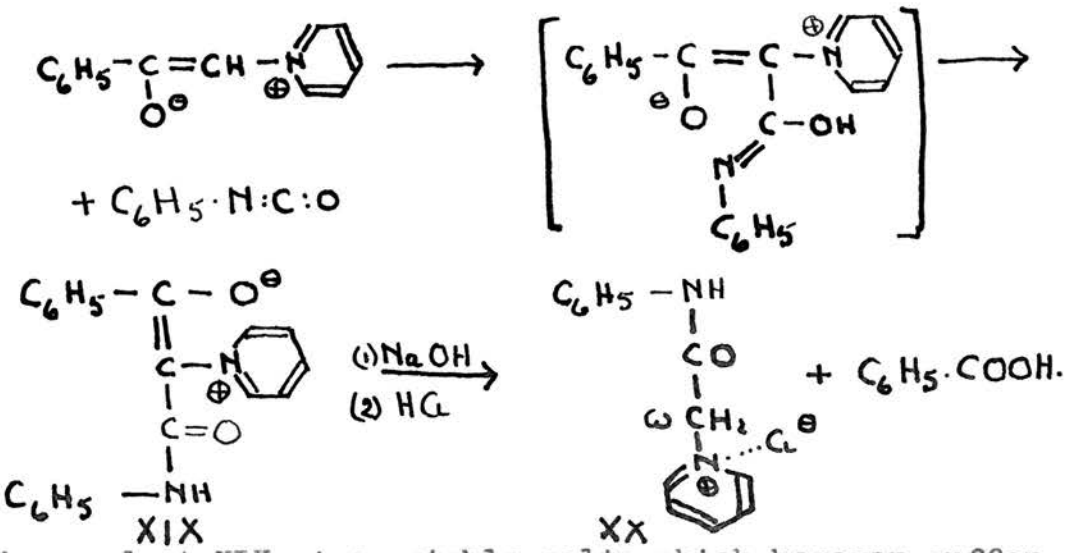
containing a reactive hydrogen atom. A Zerewitinoff active hydrogen atom determination confirmed the presence of one active hydrogen atom per molecule (Kröhnke and Kübler, Ber., 1937, 70, 538). The hydrogen atom is also readily replaced by acyl groups when the betaines react with acid chlorides or anhydrides (Kröhnke, Ber., 1935, 68B, 1177-95; Ber., 1937, 70B, 1114).



The condensation reactions of these compounds are most significant and are exactly analogous with the reactions of 1:3-diketones and β-ketoesters. The betaines themselves react, but the phenacyl pyridinium halides may be used instead, together with one molecular proportion of alkali. In addition to the reaction with benzaldehyde and acid anhydrides other typical reactions are:

(1) With isocyanate (Kröhnke and Kübler, Ber., 1937, 70B, 538)

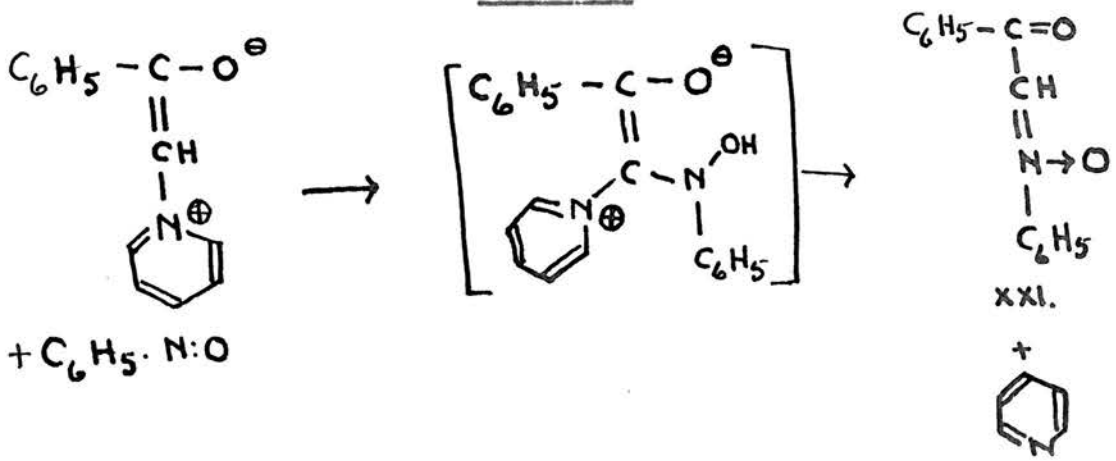
Scheme 3



The product XIX gives stable salts which however suffer acid cleavage in the presence of alkali and an acidification give benzoic acid and a acetanilide-ω-N-pyridinium halide XX, Scheme 3).

(2) With nitroso compounds (Kröhnke and Börner, Ber., 1936, 69B, 2006-16).

Scheme 4



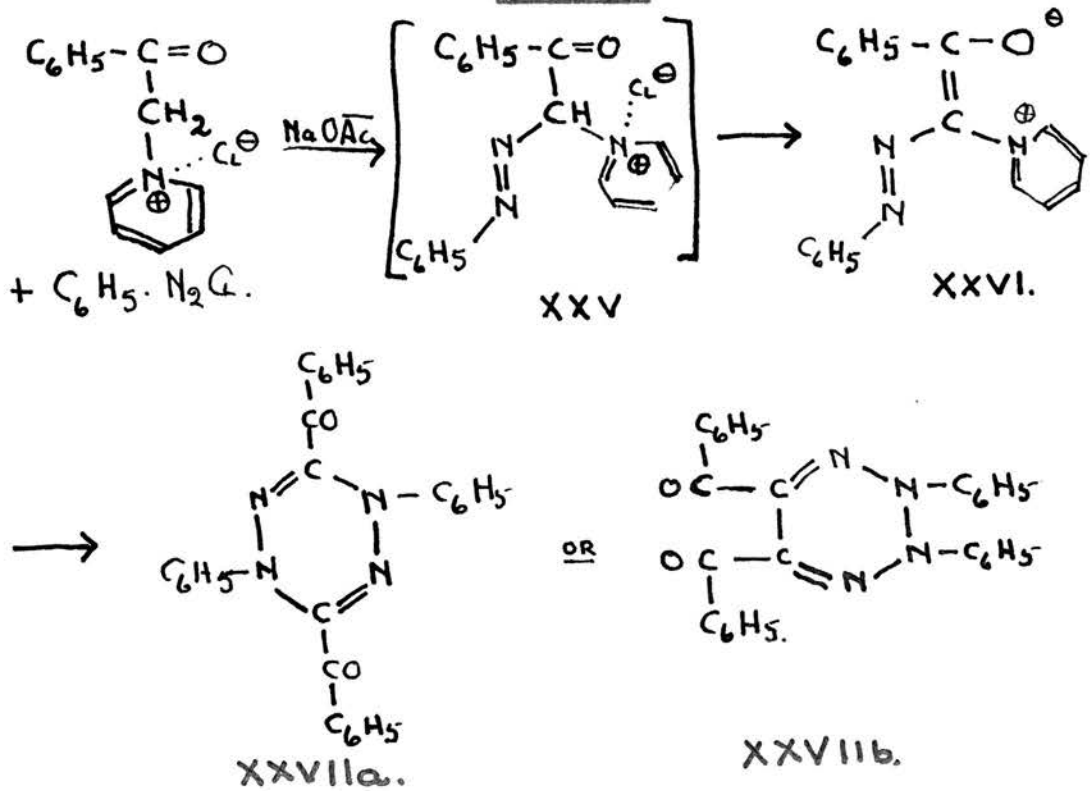
The nitrone, XXI, when treated with acid gives phenylhydroxylamine, XXII, and benzoylformaldehyde, XXIII. Alkali gives benzoyl formic acid, XXIV, and an azoxy compound.

$C_6H_5.NH.OH$ XXII $C_6H_5.CO.CHO$ XXIII $C_6H_5.CO.COOH$ XXIV

(3) With benzenediazonium salts (Krollpfeiffer and Braun, Ber., 1937, 70B, 89-95).

The coupling of phenacyl pyridinium halides with benzene diazonium halide in the presence of sodium acetate gives the phenylazo-(phenyacyl pyridinium)-halide, XXV. This on treatment with alkali gives the betaine, XXVI, which, on heating, loses pyridine forming a tetrazine of structure XXVIIa or XXVIIb (cf. Neber & Wörner, Ann. 526, 173-87).

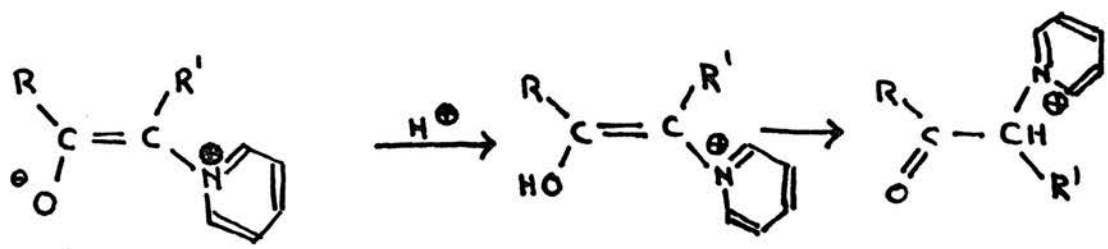
Scheme 5



Although the betaine from phenacyldimethylphenylammonium chloride is similar in structure to the methine enolbetaines of the pyridine series it is not a true methine betaine. It does not give the picrylchloride or chloranil reactions nor does it undergo reaction with isocyanates, aldehydes or diazonium compounds. It does, however, react with nitrosobenzene to give XXI by loss of dimethylaniline. The difference is therefore only one of degree of reactivity.

The basisity of the enolbetaines

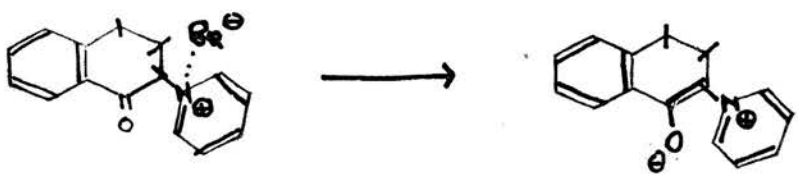
The methine enolbetaines are very basic substances even dissolving in water to give colourless solutions when carbon dioxide is bubbled through an aqueous suspension. This basicity is associated with the enol group and occurs not only in the methine enolbetaines but also in ω-alkylphenacyl-pyridinium enolbetaines of the general structure XXVIII.



R' = an alkyl group XXVIII

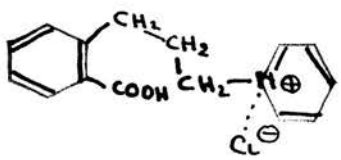
The ω -alkylphenacyl pyridinium enolbetaines

These compounds, of general formula XXVIII, resemble the methine enolbetaines not only in basicity but in their melting characteristics, colour and ability to form hydrates. Their chemical properties differ from those of the methine enolbetaines because the reactive hydrogen atom has been replaced by an unreactive alkyl group thus preventing the condensation reactions and the complex formation with chloranil and picrylchloride. A member of this group has been examined with some thoroughness by Krollpfeiffer and Müller (Ber., 1935, 68B, 1169) viz. 1-tetralone-2 N- pyridinium enolbetaine, XXX, which was derived from 1-tetralone-2N-pyridinium bromide, XXIX, in the usual way.

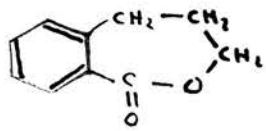


XXIX XXX

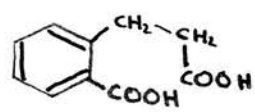
This compound was isolated apparently in a hydrated form and, as is so often experienced with the hydrates, a satisfactory analysis was difficult to obtain. Alkaline treatment followed by acidification was shown to yield (by normal acid cleavage) ω-(O-carboxyphenyl)-n-propyl-N-pyridinium chloride XXXI.



XXXI



XXXII



XXXIII

This on distillation gave the lactone of θ-carboxyhydrocinnamyl alcohol, XXXII, and oxidation of XXX with hydrogen peroxide gave θ-carboxyhydrocinnamic acid, XXXIII, (cf. page 210 for the corresponding 1-hydrindone-2N-pyridinium enolbetaine).

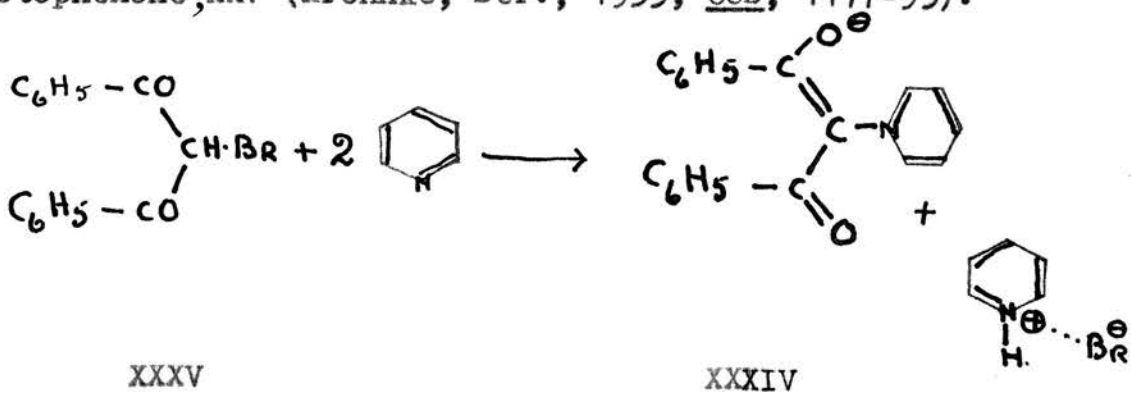
The ω -acylphenacylpyridinium enolbetaines

C-Benzoyl-phenacyl pyridinium enolbetaine, XXXIV, has been prepared by three methods:

(1) By reaction of phenacyl pyridinium enolbetaine with benzoic anhydride.

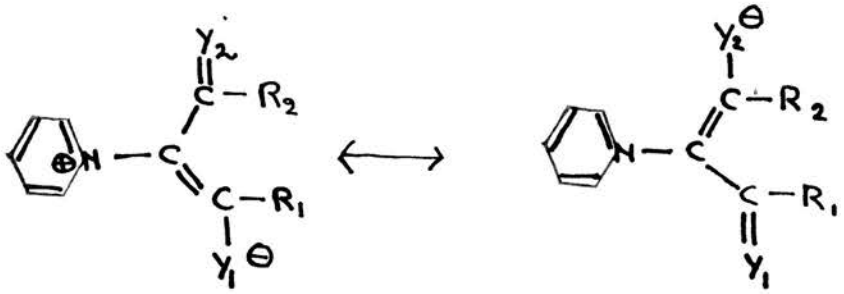
(2) By reaction of phenacyl pyridinium enolbetaine with benzoyl chloride.

(3) By the action of pyridine on -bromo- -benzoyl-acetophenone, XXV (Kröhnke, Ber., 1935, 68B, 1177-95).



XXXV XXXIV

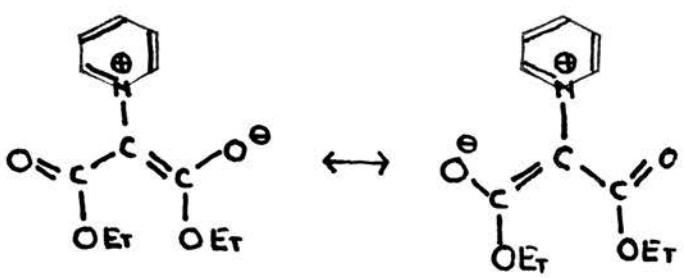
Kröhnke swiftly realized that compounds similar to XXXIV, i.e. of general formula XXXVI are capable of the mesomerism shown



XXXVI

This was supported by Kröhnke's discovery that any attempt to synthesise compounds possessing the structures of the two canonical forms gave only one product, e.g. the reaction of p-bromobenzoic anhydride with phenacyl pyridinium enolbetaine gave the same product as the reaction of benzoic anhydride with p-bromophenacyl enolbetaine.

Kröhnke prepared several compounds of this type and one of the most novel was that derived from malonic ester-2N-pyridinium bromide, XXXVII (Ber., 1937, 70B, 543).



XXXVII

Compounds of this general type are, as would be expected, very different from the enolbetaines previously described.

(1) They are less reactive and do not give the same colour reactions or condensation reactions.

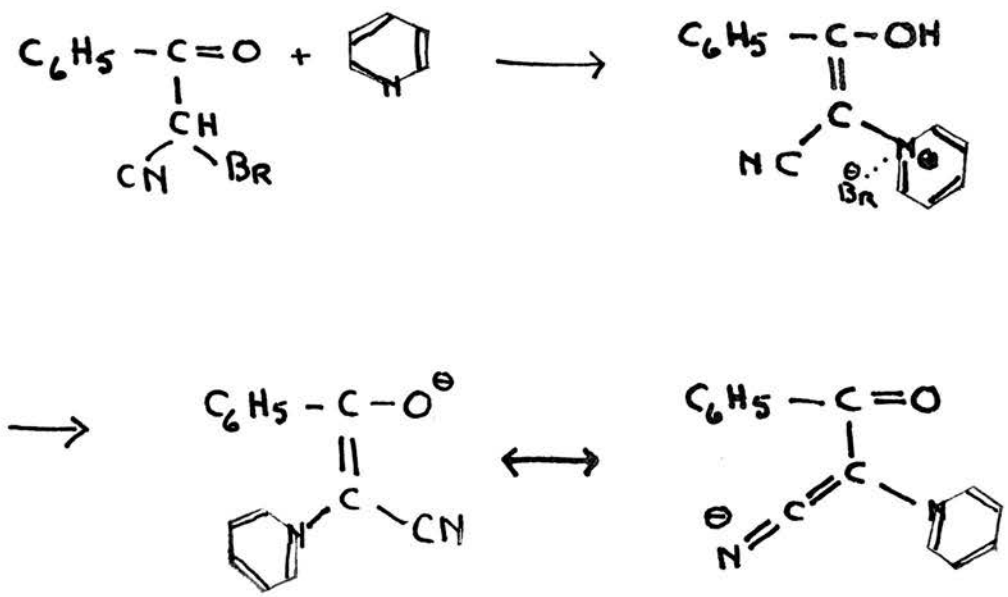
(2) They are more stable.

(3) They are high melting.

(4) They have higher solubilities in non-polar solvents.

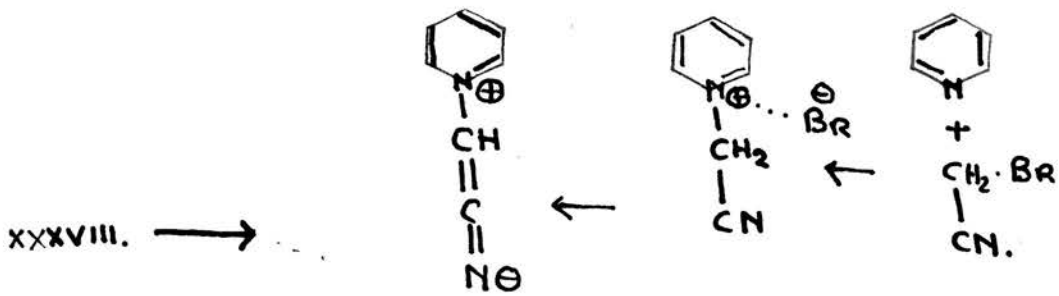
(5) They are neutral.

Several variations of this type of compound are known; for example Kröhnke prepared ω -cyanophenacyl pyridinium enolbetaine, XXXVIII (Ber., 1939, 72B, 83-9) in the usual way.



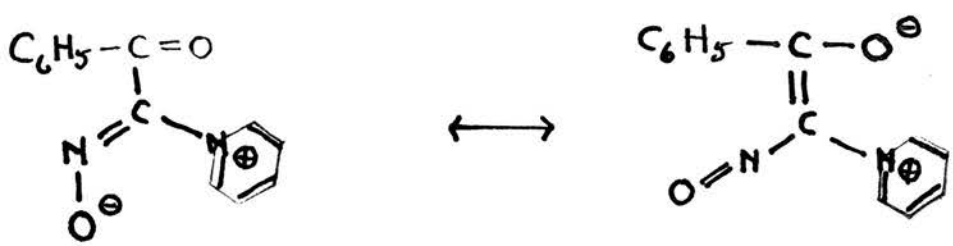
XXXVIII

This betaine suffered acid cleavage to yield the betaine, XXXIX, which was also prepared by the action of alkali on ω -cyano-N-methyl pyridinium bromide.



XXXIX

A less clearly defined case was that of the ω -nitrosophenacyl pyridinium enolbetaine, XL, obtained by the action of alkyl nitrites on phenacyl pyridinium enolbetaine in the presence of alkali (Kröhnke, Ber., 1937, 70B, 1117-20).



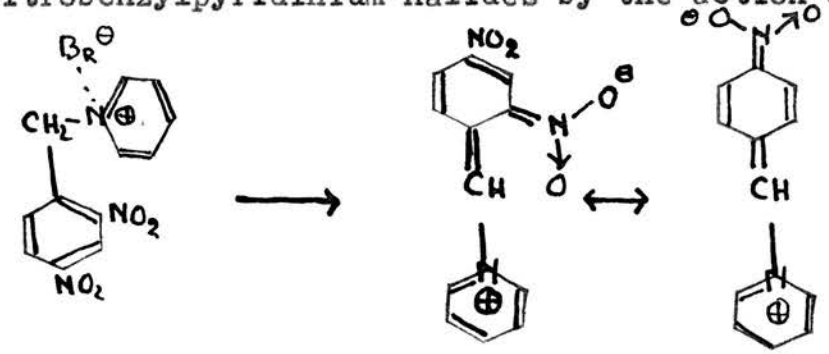
XLa XLb

The compound was extremely unstable and Kröhnke claimed the isolation of an isomer, postulating that these were the stereoisomers XLa and XLc.

XLa XLc

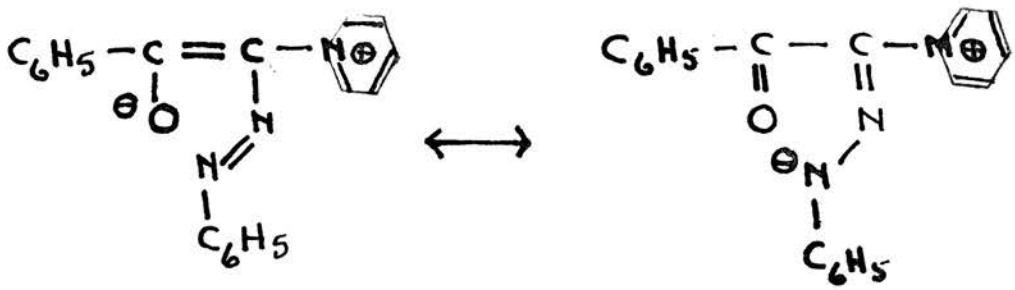
If it is true then mesomerism involving significantly, XLb, is improbable as this would tend to alter the character of $>C=N$ group responsible for any stereoisomerism. This might well be true for the relative contributions of the enolbetaine form and the oximinobetaine form might depend on the acidity of the enol ion compared with oximino ion.

Kröhnke and Schmeiss (Ber., 1937, 70B, 1118-9) have synthesised another group of pyridinium betaines, the acinitrobetaines, e.g. XLI, which were derived from polynitrobenzylpyridinium halides by the action of alkali



XLI

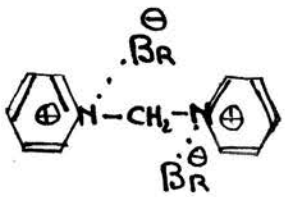
In this group of miscellaneous betaines must be included XXVIa (page 200).



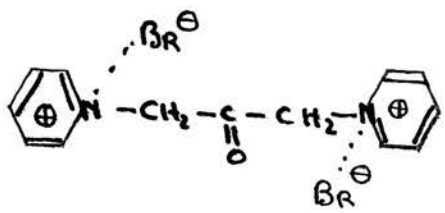
XXVI(a) XXVI(b)

Although Krollpfeiffer discussed the alternative structure XXVI(b) he concluded that XXVI(a) was the correct one and that XXVI(b) was the structure only in the case of the product from p-nitrobenzene diazonium chloride. In the light of modern resonance theories both the above structures must contribute to the resonance hybrid. A substituent, such as a nitro group, will influence the structure of the final hybrid only in so far as it affects the energy of the canonical forms and therefore their contribution to the resonance hybrid.

In recent papers Kröhnke and Lüderitz (Ber., 1950, 83, 50-9; 60-6) have continued their investigation of the enol-betaines. Their work is now concerned with the dipyridinium compounds such as XLII and XLIII.



XLII



XLIII

Enolbetaines in the hydrindene series

While attempting to prepare indone by the dehydrohalogenation of 2-bromo-1-hydrindone with pyridine a compound XLIV of the enolbetaine type was obtained (v. page 180). This compound has been investigated in some detail. The significant properties are:

(1) It forms hydrates.

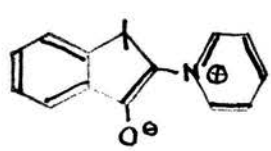
(2) The colour becomes more intense as the degree of hydration decreases.

(3) It forms a mercurichloride.

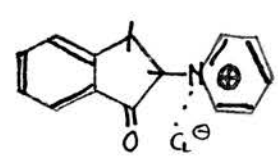
(4) It is oxidised by alkaline peroxide to homophthalic acid, XLV.

(5) By treatment with hydrochloric acid the 1-hydrindone-2N-pyridinium chloride, XLVI, is generated.

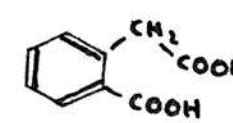
(6) It is unstable to ultra-violet light.



XLIV



XLVI



XLV

On recrystallising from aqueous methanol of differing concentrations various hydrates are formed. Three have in fact been isolated. From 10% methanol a dark red compound was obtained analysing approximately for the hemihydrate.

An orange dihydrate is obtained from a solvent 70% water, 30% methanol. An even more highly hydrated form is obtained from hot water on slow crystallisation but it is unstable in air and changes from pale orange to orange on standing a short time. The analyses of these compounds are disappointing but the problem of hydration makes the achievement of a uniform product difficult. It is very probable that the less hydrated forms are unstable and suffer aerial oxidation especially when exposed to light, for they darken in colour and their solutions in acid are then slightly coloured.

In agreement with Kröhnke's observation (page 197) the less hydrated form is more highly coloured than the more hydrated forms.

The betaine is more soluble in hydroxylic solvents (alcohols and water) than the less polar solvents such as benzene, chloroform and ether. It is fairly soluble in dioxan but the compound is decomposed after short standing probably due to oxidation by the dioxan peroxide. The betaine dissolves in dilute acetic acid and in dilute mineral acids giving colourless solutions which fluoresce green under the ultra-violet lamp. The alcohol solutions are red when concentrated and yellow when dilute and do not fluoresce in ultra-violet light. If the solid is left a few days in daylight and is then dissolved in acid the solution obtained is not completely colourless.

The betaine forms a white mercurichloride which is very insoluble. It has not been analysed because

(1) It could not be crystallised, or purified by digestion with hot solvents owing to decomposition to a yellow or orange compound.

(2) It gave no sharp melting point or decomposition point.

(3) Its homogeneity could not be guaranteed.

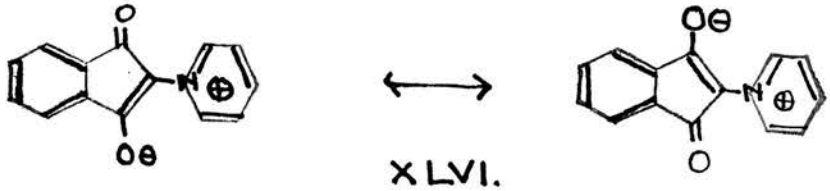
The oxidation of the betaine by peroxide to homophthalic acid was readily achieved (page 218). This oxidation is exactly analogous to the oxidation of 1-tetralone-2-pyridinium enolbetaine to O-carboxy hydrocinnamic acid (Krollpfeiffer and Müller, loc. cit.).

The formation of a compound containing the hydrindone structure by the action of acid was shown by absorption spectra. On examining the absorption spectra of the betaine in N/10 alcoholic HCl solution, an absorption curve almost identical with that of hydrindone was obtained. (See Section on absorption spectra).

The compound was found to be unstable to light of wavelength shorter than c. 5000A°. On attempting to determine the absorption curve of the compound in alcohol and water solution very large deviations from the Lambert-Beer Law were discovered. This was found to be due to a photochemical change. The yellow solution (Conc = M/1000 M/5,000) were rapidly bleached on exposure to the

ultra-violet light of the arc of the absorption photometer. No correlation between exposure time, concentration and extinction value could be made other than qualitatively owing to the difficulty of establishing reproducible conditions. These problems are discussed in the section on absorption spectra.

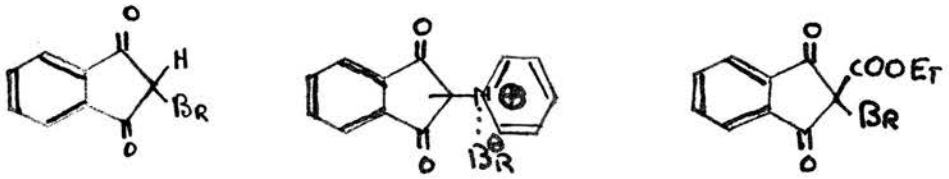
The enolbetaine, XLVI, derived from 1:3-diketohydrindene-2-pyridinium bromide, XLVII, should provide an interesting comparison with this 1-hydrindone-2N-pyridinium enolbetaine.



XLVI.

The synthesis of this compound has been achieved and its properties determined.

As 2-bromo-1:3-diketohydrindene, XLVII, has only been obtained in reasonable yield from 2-carbethoxy-2-bromo-1:3-diketo hydrindene, XLVIII, an alternative route to IV was explored which used 1:3-diketohydrindene, a small



XLVII XLIX. XLVIII

quantity of which was available. Pyridine and bromine together form an effective brominating agent (cf. Vona & Merker, J. Org. Chem., 1949, 14, 1048). If the derived bromo-compound readily forms a pyridinium bromide, then it would be reasonable to assume that the action of bromine in pyridine on 1:3-diketohydrindene should yield XLVII the 1:3-diketohydrindene 2-pyridinium bromide, XLIX. This was found to be the case and on making an aqueous solution of the pyridinium compound alkaline the desired enolbetaine XLVI, was obtained.

The salient properties of this enolbetaine are:

(1) It does not form hydrates readily.

(2) It is much more stable compared with 1-hydrindone-2N-pyridinium enolbetaine.

(3) It is higher melting than 1-hydrindone-2N-pyridinium enolbetaine.

(4) It is neutral.

(5) It is not so readily oxidised as 1-hydrindone-2N-pyridinium enolbetaine.

(6) It is fairly soluble in non-polar solvents as well as polar solvents.

(7) It does not form a mercurichloride.

(8) It is stable to ultra-violet.

The compound is soluble in alcohol and on cooling elongated prisms of a lustrous golden colour are deposited. The

addition of water to the alcohol solution precipitates the anhydrous compound. The melting point is sharp, m.p. 256°C, and slight decomposition occurs but not so intensively as in the case of 1-hydrindone-2N-pyridinium enolbetaine.

The solutions of the compound, XLVI, in dilute mineral acids are not colourless and the absorption curve (page 230) of a solution in alcohol containing sufficient hydrochloric acid to be N/10 was identical with the curve of a solution of identical concentration in alcohol but containing no acid.

Oxidation with alkaline peroxide is very slow, and pyridine is evolved but the other product - which should have been phthalic acid - could not be isolated as the work was done on a small scale, and the solubility of the phthalic acid made isolation difficult.

The compound is soluble in alcohols, glacial acetic acid and to a slight extent in water. It is fairly soluble in hot benzene, chloroform and ether and was recovered when a dioxan solution was diluted with water.

The enolbetaine was dissolved in alcohol and was added to an alcoholic solution of mercuric chloride. No precipitate was observed. That no soluble complex was formed was confirmed from the absorption spectra of the compound in alcohol solution containing 10 gms mercuric chloride per litre (page 230). The maximum at 2385 A°

($\text{Log}_{10}\varepsilon_{max} = 4{\cdot}45$) could not be observed owing to the fact that the mercuric chloride absorbed completely below 2,600A°. However at wavelengths longer than 2600A° the absorption curve was identical with that of the compound in pure alcohol.

The absorption spectra of the compound was easily found and no divergence from the Lambert Beer Law were detectable. The compound is more stable to light than the 1-hydrindone-2-pyridinium enolbetaine.

Although the true extinction values of the 1-hydrindone-2-pyridinium enolbetaine were not found owing to the bleaching of the solutions it was apparent that the $\log_{10}\varepsilon$ Max values are higher for XLVI than XLIV.

Experimental

1-Hydrindone-2N-pyridinium enolbetaine

2-Bromo-1-hydrindone (2·1 gms, page 180) was dissolved in dry pyridine (5 mls) and the clear solution was warmed for one minute at its boiling point. The brown opaque mixture was poured into cold water (20 mls) and the excess pyridine was removed by ether extraction. The aqueous layer was made alkaline with cold caustic soda solution (2N). Immediate separation of orange needles 1·7-8 gms) occurred and they were recrystallised from aqueous methanol.

(1) Solvent 10%H_2O:90%CH_3OH. The compound crystallised as irregular rhombic prisms.

$C_{14}H_{11}NO$ requires 80·2%C; 5·3%H; 6·7%N.

$(C_{14}H_{11}NO)_2,H_2O$ requires 77·0%C; 5·5%H; 6·4%N.

Found 76·4%C; 5·6%H; 5·6%N.

(2) Solvent 70%H_2O: 30%CH_3OH. The compound crystallised as slender orange needles.

$C_{14}H_{11}NO$, $2H_2O$ requires 68·6%C; 6·2%H.

Found 68·9%C; 5·6%H.

(3) Compound 2 after drying. The compound retained the crystal form but was red in colour.

$(C_{14}H_{11}NO)_2H_2O$ requires 77.0%C; 5.5%H; 6.4%N.

Found 75.5%C; 5.8%H; 5.5%N.

Cf. analysis for 1-tetralone-2N-pyridinium enolbetaine (Krollpfeiffer and Müller, loc.cit.).

Found 73.5-74.2%C; 5.9-6.3%H; 6.1%N.

Required 74.7%C; 6.2%H; 5.8%N.

The melting point depended on the rate of heating; loss of water of crystallisation occurred above 100° and decomposition occurred after 150°C. Melting occurred at 170°C when rapidly heated and at 166°C when slowly heated.

Oxidation of 1-hydrindone-2N-pyridinium enolbetaine

1-Hydrindone-2N-pyridinium enolbetaine (0·1 gms.) was dissolved in a mixture of perhydrol (0·5 mls.) and caustic soda solution (1 ml, 1N) with warming. The colour disappeared rapidly and the solution was then acidified. After 24 hours a white crystalline compound (0.035 gms.) was removed by filtration and after recrystallisation from aqueous methanol, it had a melting point of 180-1°C. Homophthalic acid has a melting point of 183°C. Mixed melting point with authentic sample 182-3°C.

$C_9H_8O_4$ required 60.0%C and 4.5%H;

Found 59.5%C and 4.5%H;

The mercurichloride of 1-hydrindone-2N-pyridinium enolbetaine

On adding a solution of the enolbetaine in alcohol to a solution of mercuric chloride in alcohol (10 gms per litre) a white precipitate was obtained. This solid became yellow

when warmed in solution or when warmed at 30°C. It did not melt sharply so it was not analysed, especially as it could not be crystallised or even digested with hot solvents without darkening.

Sensitivity: On mixing equal volumes of solutions of the enolbetaine (Conc. = M/5000) and of mercuric chloride (10 gms./litre) an opacity was observed. Rapid coagulation occurred and a clear colourless solution was left.

1:3-diketohydrindene-2N-pyridinium enolbetaine

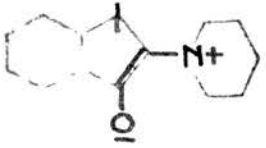
A solution of bromine (0·75 mls.) in pyridine (5 mls.) was added to 1:3-diketohydrindene (1.46gms.) dissolved in pyridine (2mls.). Some heat was developed and finally the mixture was warmed to 80°C before being poured into water (100 mls.). The excess pyridine was extracted with ether and the coloured water layer was made alkaline with 2N caustic soda solution. On standing, the dark solution deposited yellow plates which, when filtered, formed a gleaming yellow mat on the filter paper. Recrystallisation from ethanol gave elongated prisms (0.5 gms.) with a yellow metallic lustre. M.p. 255-6°C (decomposition).

$C_{14}H_9O_2N$ requires 75.3%C; 4.1%H; 6.3%N.

Found 74.5%C; 3.9%H. 6.2%N.

Oxidation of 1:3-diketohydrindene-2N-pyridinium enolbetaine

The conditions employed were identical with those employed on 1-hydridone-2N-pyridinium enolbetaine. The colour was in this case very much slower in disappearing. Pyridine was evolved in the vapour but acidification of the colourless solution did not give any solid acid.



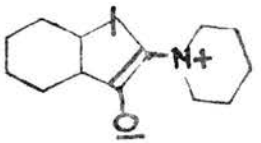


FIG 1.

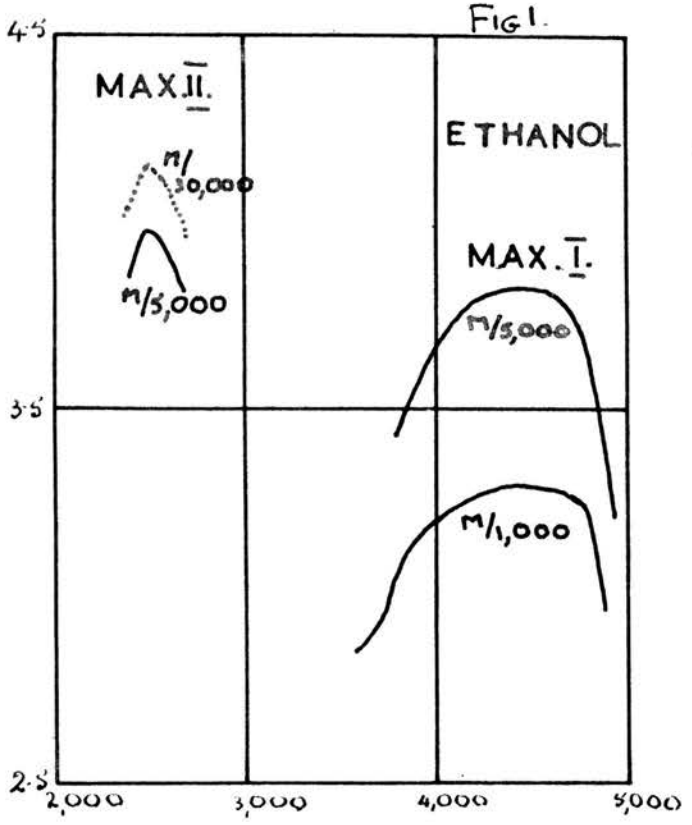
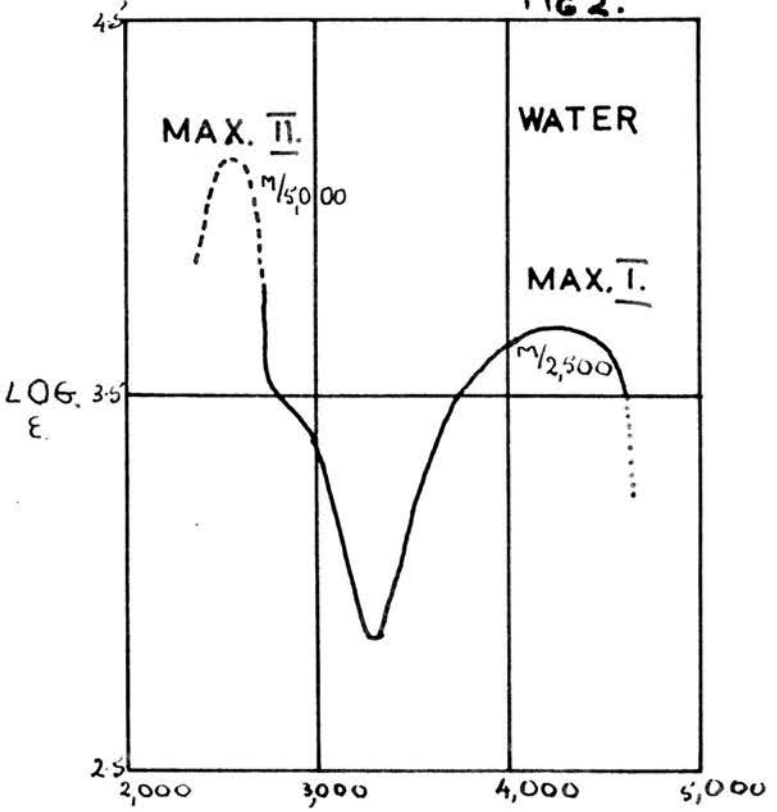


TABLE I.

CONC.	IDEAL LOG. $\varepsilon_{max.}$	EXPOS. TOTAL
m/5,000	3·82	67 SECS.
m/1,000	3·29	353 SECS.

FIG 2.



MAX.	λ	LOG. ε.
	4,250	3·68
II	2,570	4·14

The Absorption Spectra of the Enolbetaines of the Hydrindene Series

(a)

1-Hydrindone-2N-pyridinium enolbetaine

The absorption spectra in fig. I show the results of an attempt to evaluate the molar extinction coefficients of the absorption maxima of 1-hydrindone-2N-pyridinium enolbetaine in alcohol solution. On attempting to determine $(\log_{10}\varepsilon_{max})_{4,400}$ grave discrepancies from the Lambert-Beer Law were observed. The difference between the values of $(\log_{10}\varepsilon_{max})_{4,400}$ with the concentration M/1000 and M/500 is 0.53. Ideally it should be zero. It was observed that the yellow colour of the solutions in the cell faded and became almost colourless during the period of exposure to the arc indicating a photochemical reaction. The greater the extent of the reaction, the smaller will be the calculated value of $(\log_{10}\varepsilon_{max})_{4,400}$.

If the following assumptions are made then a semi-quantitative analysis of the results tabulated opposite is possible. They are

(1) That there is a negligible induction period.

(2) That the reaction products do not absorb at 4,400 Å.

(3) That the reaction is not an oxidation by dissolved oxygen.

The reaction may be unimolecular, pseudounimolecular or bimolecular. It is unlikely to be of a higher order. If it is unimolecular or pseudounimolecular then the velocity constant, K, of the reaction is given by

$$K = \frac{1}{t} \log {}^{C_o}/_{C_t} \qquad \ldots(\alpha_1)$$

where C_o is the initial concentration and "C_t" is the concentration after time "t". If the reaction is bimolecular then with a similar nomenclature

$$K = \frac{1}{C_o t} \cdot \frac{C_o - C_t}{C_t} \qquad \ldots(\beta_1)$$

When $C_o = M/1000$ $\quad t_{max} = 350$ secs.

When $C_o = M/5000$ $\quad t_{max} = 67$ secs.

Substituting these values the relationships α_1 and β_1 are transformed into α_2 and β_2 respectively

$$(\alpha_1) \quad a.K = M/350 \cdot \log_{10}(M/1000C'_t) = 1/67 \cdot \log_{10}(M/5000C''_t) \qquad \ldots(\alpha_2)$$

where "a" is a factor to alter the logarithmic base

$$(\beta_1) \quad K = \frac{1000}{350} \times \frac{1-1000C't}{1000C't} = \frac{5000}{67} \times 1 - \frac{5000C''t}{5000C''t}$$

$$\text{i.e.} \quad \frac{1-1000C't}{350C't} = \frac{1-5000C''t}{C''t} \qquad \ldots(\beta_2)$$

In these equations C_t' and C''_t are the concentrations corresponding to the initial concentrations $C_o = M/1000$ and $C_o = M/5000$ and the times 350 secs. and 67 secs. respectively.

If a further relationship between C'_t and C''_t can be found then it should be possible to evaluate them on the assumption that the reaction is (α) unimolecular or (β) bimolecular by the solution of the appropriate equations. C'_t and C''_t can be readily related in the following manner. If the values C'_t and C''_t had been used with the appropriate values D' and D, of the optical density of the solutions then the true value of $(\log_{10} \varepsilon_{max})$ would have been obtained in each case, i.e.

$$(\log_{10}\varepsilon_{max})^{True}_{4400} = \log_{10}D' - \log_{10}C'_t = \log_{10}D'' - \log_{10}C''_t \quad \ldots(3)$$

Now on the assumption that the conditions were ideal C_o' and C''_o were used instead of C'_t and C''_t . The departure from ideality, Δ , is given by

$$\Delta = (\log_{10} max)'_{4400} - (\log_{10} max)''_{4400} = \log_{10}D' - \log_{10}C'_o - \log_{10}D'' + \log_{10}C''_o \quad \ldots(4)$$

$$\therefore \Delta = (\log_{10}D' - \log_{10}D'') - (\log_{10}C'_o - \log_{10}C_o'') = \log_{10} D'/D'' - \log_{10} C_o'/C_o'' \quad \ldots(5)$$

Now from (3) $\log_{10}D'/D'' = \log_{10}C_t'/C_t''$ ...(6)

$$\therefore \Delta = \log_{10} C_t'/C_t'' - \log_{10} C_o'/C_o'' = \log_{10} \frac{C_t'\, C_o''}{C_t''\, C_o'} \quad \ldots(7)$$

Now when $C_o' = M/1000$ and $C_o'' = M/5000$ from fig. I $\Delta = -0{\cdot}53$

$$\therefore \log_{10} \frac{C_t'' \times 5000}{C_t' \times 1000} = 0{\cdot}53$$

$$\therefore \log_{10} \frac{5C_t''}{C_t'} = 0{\cdot}53$$

$$\text{and} \quad C_t'' = 0{\cdot}68C_t' \qquad \ldots(8)$$

By eliminating C_t'' from equations α_2 and β_2 using equation (8), C_t' and then C_t'' can both be found on the assumption that the reaction is

(α) Unimolecular when $C_t' = 2.24 \times 10^{-4}$ Moles. per litre

and $C_t'' = 1.51 \times 10^{-4}$ Moles. per litre

(β) Bimolecular when $C_t' = 2.9 \times 10^{-4}$ Moles. per litre

$C_t'' = 1.9 \times 10^{-4}$ Moles. per litre.

Now D' and D", i.e. $(\log_{10} I_o/I)'$ and $(\log_{10} I_o/I)''$ are both known (they are 1.9 and 1.3 respectively). By using these values and equations (3) $(\log_{10}\varepsilon_{max})^{True}$ may be calculated when the reaction is assumed to be

(α) Unimolecular in which case $(\log \varepsilon_{max})^{True} = 3.93$

(β) Bimolecular in which case $(\log_{10}\varepsilon_{max})^{True} = 3{\cdot}83$

Error. Now it is impossible to discover from the above argument whether the reaction is in fact unimolecular or bimolecular. It is apparent, however that the analysis gives in both cases a reasonable value for $(\log_{10}\varepsilon_{max})^{True}$.

The assumption that no induction period exists may be untenable but any error introduced cannot be assessed. The second assumption is a reasonable one for 4,400 Å is within the visible region and after prolonged illumination the solution is colourless. The above analysis could not however be applied to the maximum at 2,520 Å for any probable product might absorb in this region.

The nature of the reaction. The reaction may involve as its preliminary stage

(1) the decomposition of one molecule of the betaine.

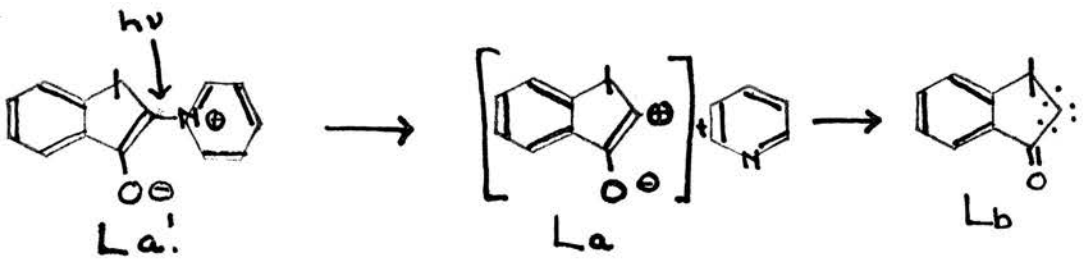
(2) the reaction of one molecule of the betaine with one of solvent.

(3) the reaction of one molecule of the betaine with one of dissolved oxygen.

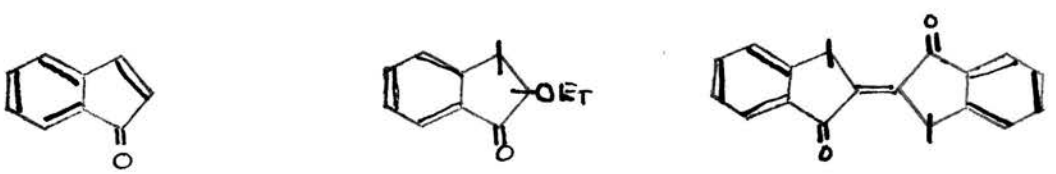
(4) the reaction of two molecules of the betaine.

The reaction kinetics of (1) would be unimolecular and of (2) pseudounimolecular. The kinetics of (3) and (4) would be bimolecular. Assumption (3) in the kinetics analysis had to be made as the concentration of dissolved molecular oxygen was unknown; however, if its concentration were of the same order as the betaine, no error would be introduced.

If the betaine decomposed unimolecularly the reaction would probably be



The initial product, La, would suffer electron shift leaving the α-carbon atom with two electrons short of a complete octet. This could then rearrange to indone, LI, or react with solvent to give 2-ethoxy hydrindone, LII, or with a molecule of betaine to give the derivative of dibenzoyl ethylene, LIII, and pyridine.



LI LII LIII

If the reaction is pseudounimolecular the product would probably be, LII, 2-ethoxy hydrindone. If, however, a bimolecular course involving dissolved oxygen was the relevant reactiona peroxide, a ketone, e.g. 1:2-diketo-hydrindene, or the anhydride of homophthalic acid might be the product. A bimolecular course would give almost certainly LIII.

In an endeavour to identify the product a relatively concentrated solution (100 mgs. per 5 mls.) was illuminated by an ultra-violet lamp for 24 hours and it became pale yellow in colour. 2:4-dinitrophenylhydrazone formation was attempted but although there was evidently some reaction, no pure product was isolated. A ketonic compound is apparently formed but whether decomposition of the initial product or polymerisation of the ketone had occurred thus presenting the effective isolation of a 2:4-dinitrophenyl hydrazone cannot yet be decided.

Conclusion. 1-Hydrindone-2N-pyridinium enolbetaine shows two prominent absorption maxima at 4,400 Å and at 2,520 Å but as it suffers photochemical change, marked deviations from the Lambert-Beer Law occurs. It is, however, probable that $(\log_{10}\varepsilon_{max})4400\text{Å}$ is of the order 3·9 and the maximum at 2520 $(\log_{10}\varepsilon_{max})\ 2520\text{Å} = 4.1$. The nature of the reaction and the products are unknown.

The absorption of 1-hydrindone-2N-pyridinium enol-betaine in aqueous solution was determined, fig. 2. The discrepancies from the Lambert-Beer Law did exist in this case also but were not of the same magnitude and it was found possible to obtain a satisfactory curve in the region 2,700Å - 3,800Å.

Table II

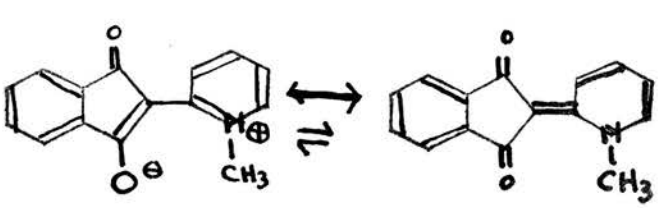
		log	Conc
Maximum$_1$	4250 Å	3.68	M/2500
Maximum$_2$	2570	4.14	M/5000
Minimum	3250	2.86	
Inflexion	2900	3.42	

Table II gives the relevant data for maxima, minimum and inflexion and in table III the wavelengths of the corresponding maxima in differing solvents are contrasted.

Table III

Solvent	Water	Alcohol
Maximum$_1$	4250 Å	4,400 Å
Maximum$_2$	2570 Å	2,520 Å

This difference is not unprecedented Kuhn and Bär (Ann. 516 158) for example when investigating the absorption of N-methylpyrophthalone, LIV, in water and in chloroform, found that in water one maximum was at 3,700 Å and in chloroform at 4,100 Å.



LIV

This difference they explained by the equilibrium above but modern resonance theory would now demand the two structures as canonical forms of the true hybrid structure. Dimroth would take this further and suggest that in different solvents, i.e. solvents of different polarity, the contributions of these canonical structures would differ, i.e. the resultant resonance hybrid for the same compound is different in differing solvents. Where Kuhn and Bär suggested an equilibrium of two forms in solution, Dimroth would suggest an effective equilibrium state between the two canonical structures dependent on the solvent. It is significant that both LIV and the enolbetaine under consideration form hydrates. It may well be that the explanation of the difference in colour of the hydrates of the enolbetaine and the differing absorption characteristics in water compared with alcohol are due to the same reason, namely the different molecular environment. As the envelope of water is increased the colour becomes less intense; that this change is associated with the influence of the polar solvent molecules on the effective dipolar structure in the Dimroth sense is quite possible.

The absorption spectra of 1-hydrindone-2N-pyridinium enolbetaine in acid solution is contrasted in fig. 3 with the absorption curve of 1-hydrindone in alcohol solution

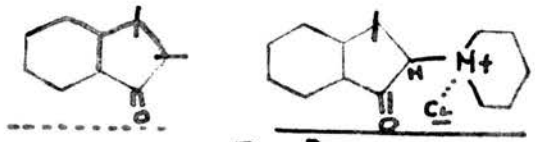
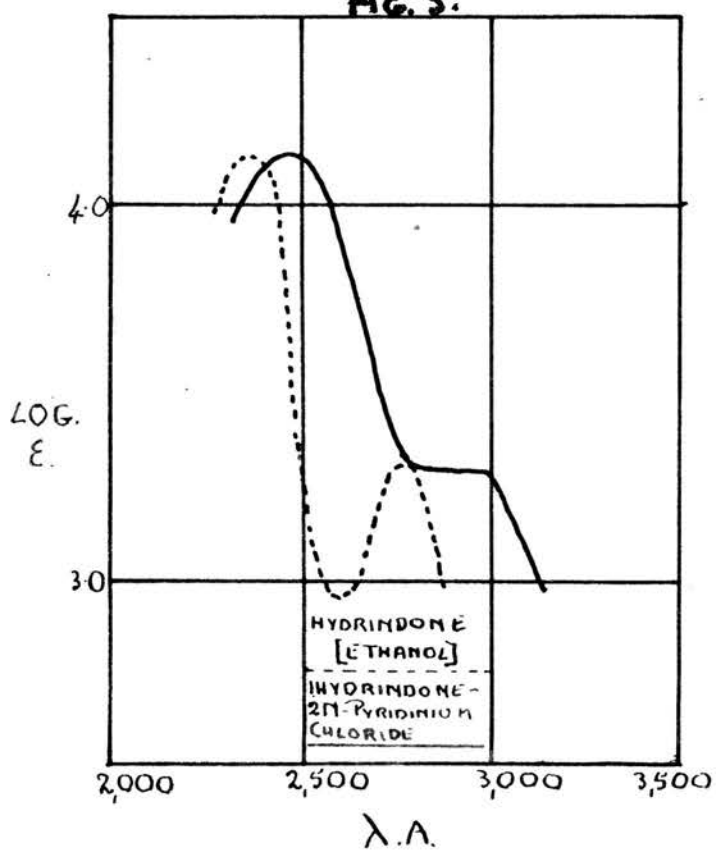
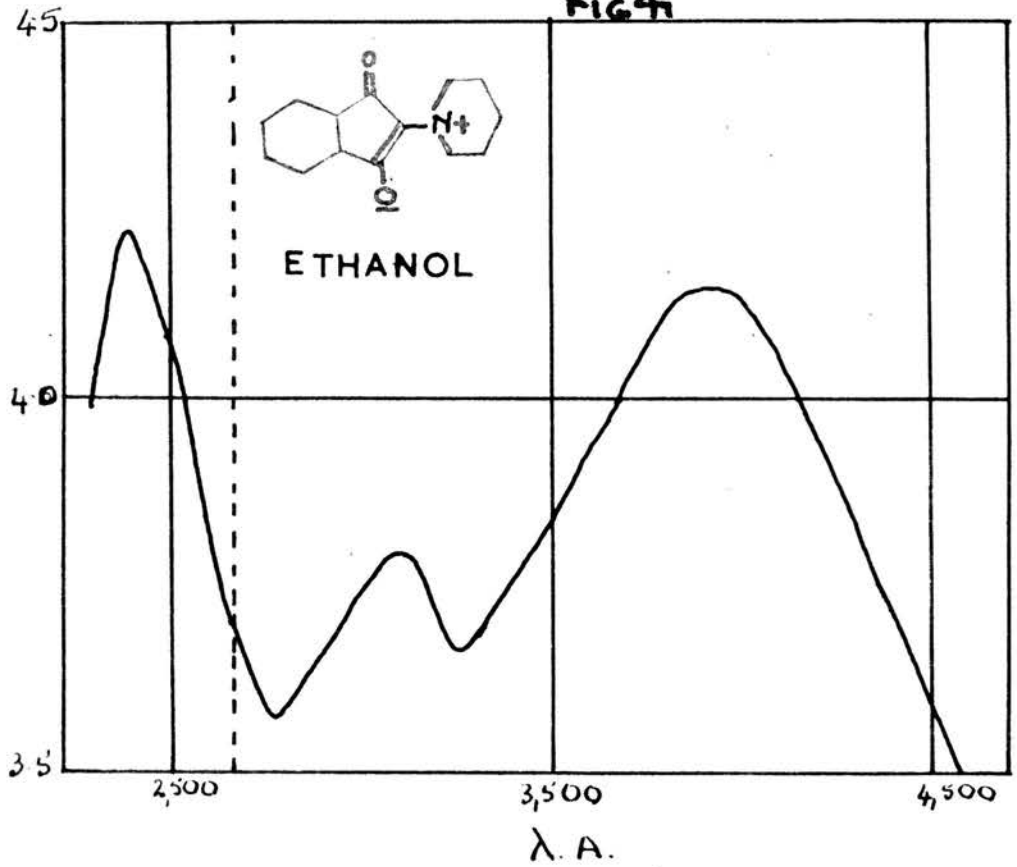


FIG. 3.



λ_{max}	Log. ε.	λ_{max}.	Log. ε.
2,350	4·13	2,470	4·14
2,750	3·32	2,800 →970	3·32

FIG 4.



$\lambda_{max.}$	Log. ε.
3,930	4·28
3,090	3·58
2,385	4·45

$\lambda_{min.}$	Log. ε.
3,250	3·31
2,760	3·14

(Ramart-Lucas and Hoch, Bull. Soc., A35, 2, 333). 1-hydrindone-2N-pyridinium chloride would be expected to absorb at slightly longer wavelengths and this is the case. The fairly close correspondence of the values of $\log_{10}\varepsilon_{max}$ for the maxima in hydrindone and the maximum and inflexion in the betaine are in accord with the accepted structure.

(b)

1:3-Diketohydrindeno-2N-pyridinium enolbetaine

This compound, absorption curve fig. 4 is stable to light and no deviations from the Lambert-Beer Law are observed. The absorption curve is not affected by making a solution in alcohol acid, (N/10), nor is it affected, beyond the expected total absorption below 2,700 Å, by incorporation of mercuric chloride (10 gms./litre). Comparison with fig. 2 shows that the general absorption pattern is the same in the case of 1-hydrindone-2N-pyridinium enolbetaine, XLIV, 1:3-diketohydrindene-2N-pyridinium enolbetaine, XLVI and N-methylpyrophthalone, LIV, Table IV

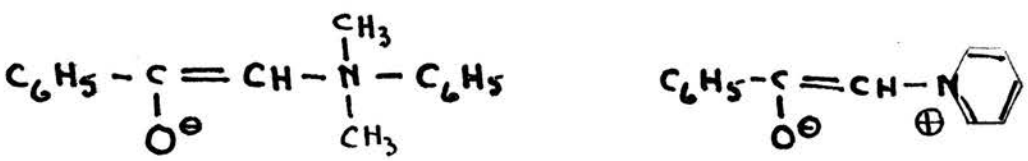
Table IV

	XLIV	XLVI	LIV
Maximum$_1$	4250	3930	4090
Maximum$_2$	3250	3090	3000
Maximum$_3$	2570	2385	2340.

The Colour of the Enolbetaines

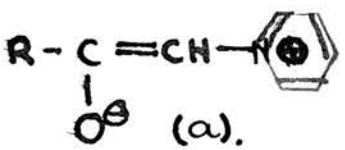
The colour of the enolbetaines has only been discussed by Kröhnke in vague terms. He realised that the colour was due both to the polar nature of the molecules and the extended conjugated system. No satisfactory explanation of the lack of colour of phenacyl dimethyl phenyl ammonium enolbetaine, XVI, has been made. In this case they realised that the molecule was an enolbetaine in spite of its lack of colour.

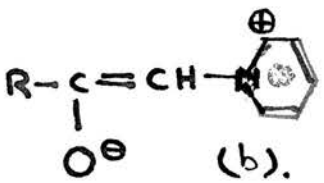
The explanation of the colour of phenacyl pyridinium enolbetaine and related compounds is apparent when the modern resonance concepts are applied to the problem. The structure XI given to this compound by Kröhnke is only one of the contributing structures.

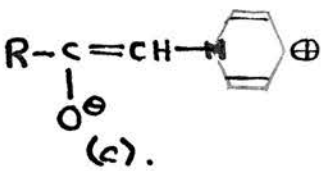


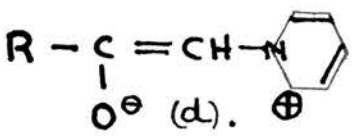
XI

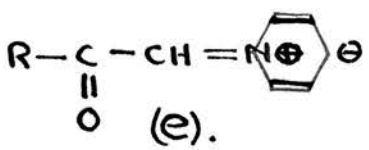
The true structure is a resonance hybrid of a series of structures of which the following are the most important.


(a).


(b).


(c).


(d).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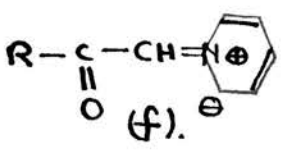
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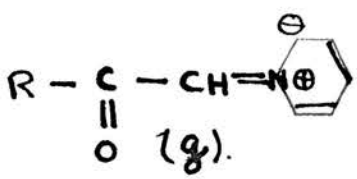
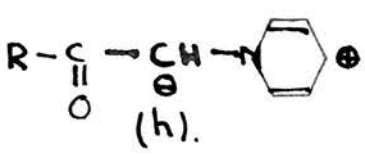
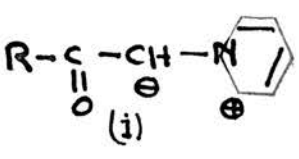
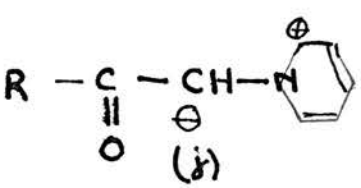

(g).


(h).


(i)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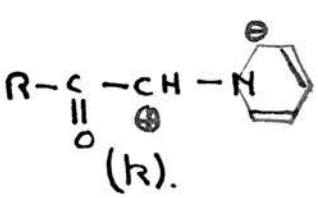
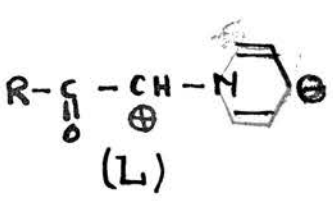
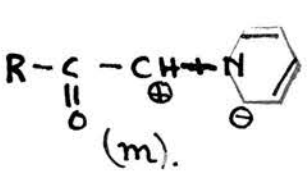

(k).

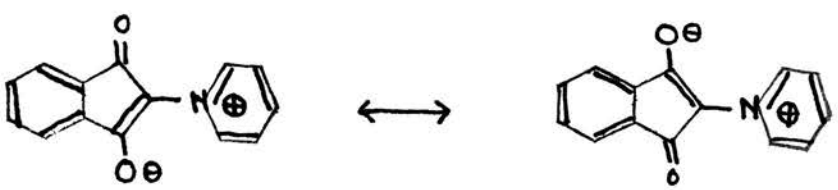

(L)


(m).

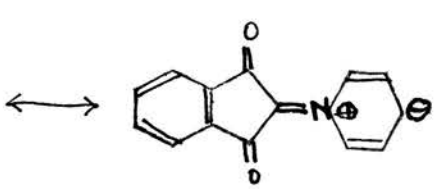
Structures (a)-(g) are probably the most important. Compounds of this type which involve resonance among a series of dipolar or polar structures are always coloured.

In the case of phenacyl dimethyl phenyl ammonium enolbetaine form XVI is the only structure which contributes significantly. The nitrogen atom is not in a closed conjugated system such as the pyridinium group and therefore the possibilities of resonance are reduced.

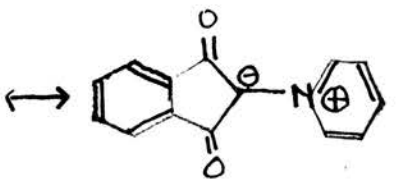
The above brief discussion of the colour applies to the methine pyridinium enolbetaines and also to the alkyl phenacyl pyridinium enolbetaines. The acyl phenacyl pyridinium enolbetaines, such as 1:3-diketohydrindene-2N-pyridinium enolbetaine, present an even more complex problem. In this case the possibilities of resonance are increased.



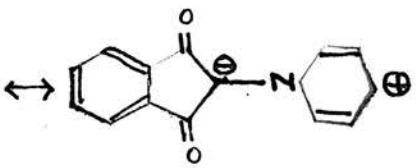
XLVI



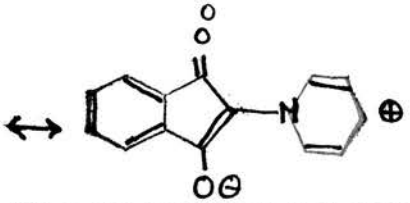
etc.



etc.



etc.



etc.

The resulting molecules would be expected at first glance to be more deeply coloured. This is only partly true. Depth of colour is defined by two factors (1) the wavelengths at which absorption of light occurs and (2) the effectiveness with which light of a particular wavelength is absorbed.

Usually when a compound is said to be more deeply coloured than another the wavelength of absorption is longer, but factor (2) is also important. The wavelength of absorption is a function of the energy change in the photo-excitation of the electronic state in the molecule. The effectiveness of the absorption, i.e. the extinction coefficient is a measure of the probability of the photo-excitation occurring. 1:3-diketohydrindene-2N-pyridinium enolbetaine absorb at slightly shorter wavelengths than 1-hydrindone-2N-pyridinium enolbetaine but its extinction coefficients are much higher than those of 1-hydrindone-2-pyridinium enolbetaine. It is however much more usual for

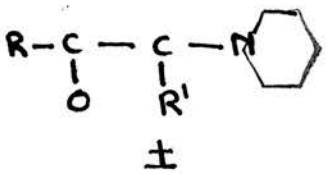
both factors, wavelength and extinction coefficient, to increase with an increase in the resonance possibilities.

The cause rests probably on a change in the essential polarity of the two types of structure. Compounds of type XI are basic - and they are basic because of the

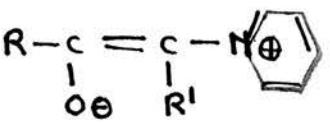
group. It is apparent that the structures in the series a-g which possess this group must play a very significant part, in the resonance. Compounds of type XLVI are however neutral. There are in this case two principal groups which share equally the development of the enolate ionic group. The basic strength of the molecule is therefore considerably reduced. The resultant polarity of the molecule will also be less than in XI. The wavelength of absorption is possibly dependent on the resultant polarity of the molecule.

Meso-ionic compounds and the Enolbetaines

Baker, Ollis and Poole (J., 1449, 307) in their consideration of the chemistry and structure of the sydnones concluded that the general structure of this group of compounds could not be represented by one covalent formula or hybrid of several covalent forms; instead the structure may only be depicted as a hybrid of several ionic forms (mostly dipolar or tetrapolar in nature). For compounds of this type the above writers coined the name meso-ionic - mesomeric/ionic. In the above mentioned paper they discuss several compounds which were previously known but which had never been satisfactorily formulated - and suggest that these compounds are meso-innic or partially meso-ionic (i.e. non-ionic covalent forms contribute to the hybrid). They do not however mention what is probably the largest known group of such compounds namely the enol-betaines. In the brief discussion of the colour of the enolbetaines it has been shown that the colour can only be understood if a resonance is postulated among a number of contributing dipolar structures. The enolbetaines therefore merit the application of the term meso-ionic. Baker, Ollis, and Poole would represent the enolbetaines as LV.



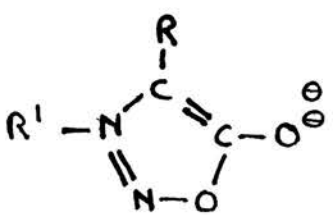
LV



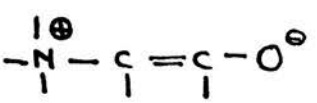
XI

But whether this is in fact preferable to the use of the principal contributing structure XI is questionable.

The enolbetaines and the sydnones are very closely related. Just as XI is the most significant contributing form in the enolbetaines so LVI is the most important form in the sydnone series (Hill and Sutton, J., 1949, ~~452~~ 746).



LVI

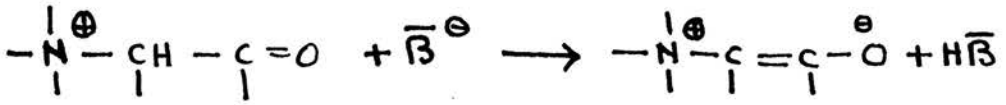


LVII

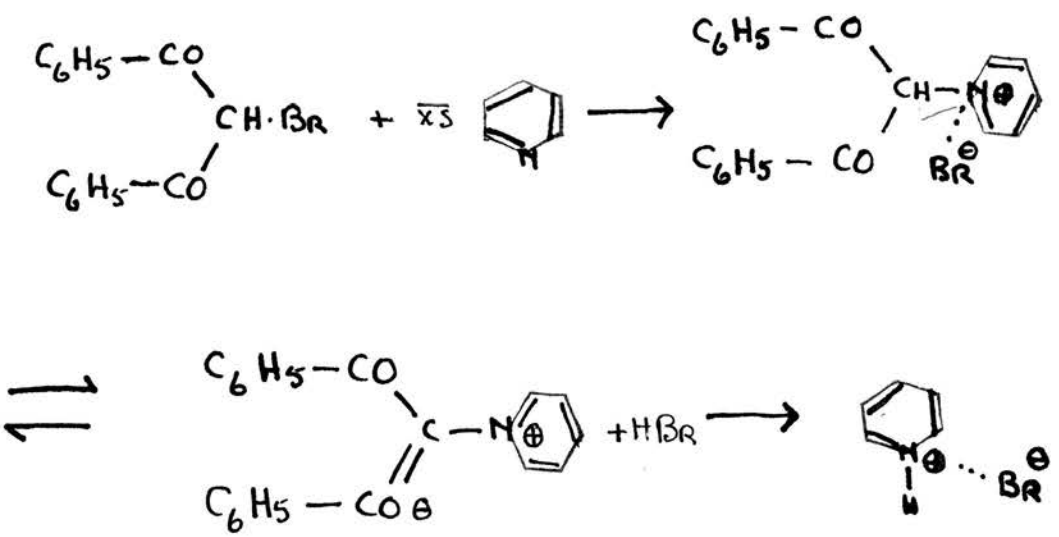
The latter contains the fundamental group of the enolbetaines namely a quaternary ionic combined with an enolate ionic group, LVII.

Kröhnke has pointed out that wherever in a molecule a quaternary nitrogen atom and an enolisable group are encountered then the possibility of enolbetaine formation

must be reckoned with. The formation of a structure of type LVII occurs according to the general pattern

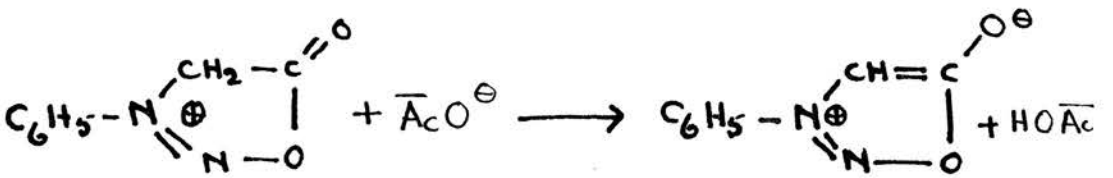


In the case of the methine enolbetaines and the ω -alkyl phenacyl enolbetaines $\overline{B}^{\oplus}$ is a hydroxyl ion but in the case of the acyl phenacyl enolbetaines it may be a halide ion thus

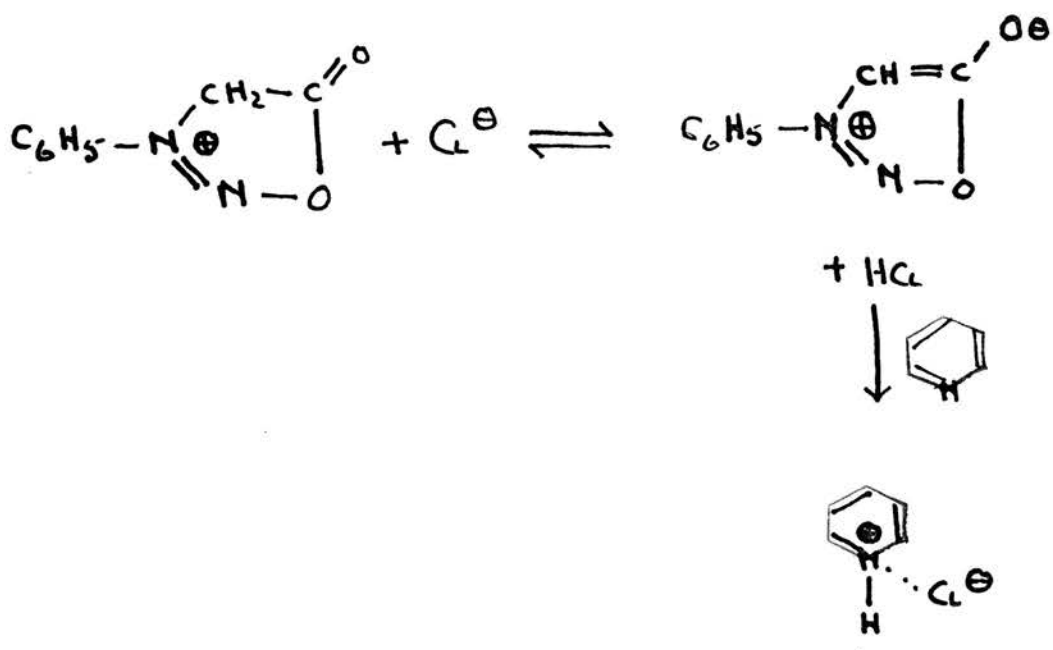


The increased acidity of the N-(diacylmethyl)-pyridinium halide permits the removal of the $H^{\oplus}$ by the basic halide ion. The reversibility of this reaction is affected by the pyridine which reacts with the hydrogen halide as it is formed.

The suggested mechanism of sydnone-formation Baker, Ollis and Poole (J., 1950, 1544) is exactly analogous to the above. The last stage in the case of the reaction of N-nitroso-N-phenylglycine with acetic anhydride, is:

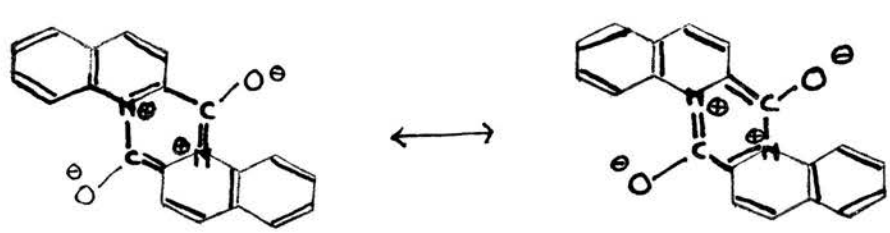


In this case the acetate ion is sufficiently basic to remove the hydrogen ion. Another significant fact that these authors failed to interpret is the reaction of N-nitroso-N-phenylglycine with thionyl chloride in (1) dry ether (yield 28% of N-phenylsydnone) and (2) in dioxan with pyridine (yield 75% of N-phenylsydnone). Here the reaction is

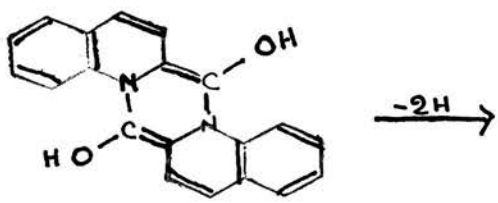


The difference in yield is explained by the pyridine removing the hydrogen chloride produced and thus influencing the equilibrium.

Another cyclic meso-ionic compound lately described is the so-called quinocoll of Hammick & Brown (J., 1950, pp. 628 et seqq.). The two principal contributing structures are



Each of these contains the enolbetaine structure. Hammick and Brown have shown that such compounds are produced by the oxidation of dihydro quinocoll LIX.

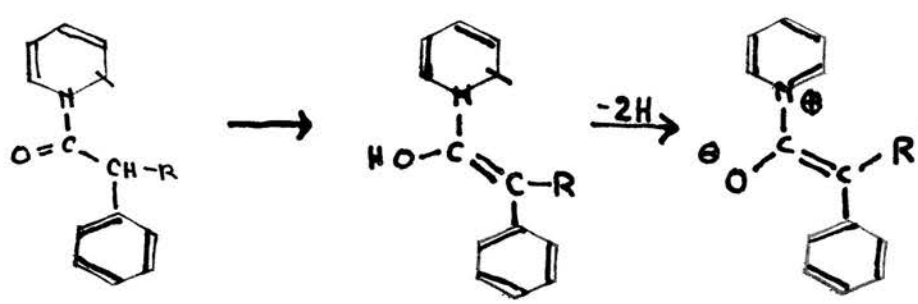


LVIII

LIX

The interesting possibility of the synthesis of other enolbetaines by an analogous route now arises.

E.g.



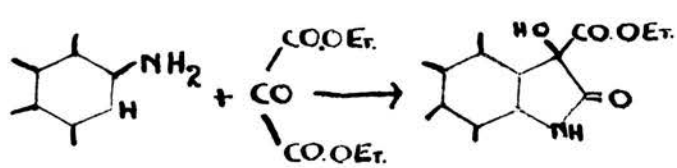
PART II

Section II (i)

The Substitution Reactions of 2-aminofluorene

Summary. The reaction of oxomalonic ester and 2-aminofluorene (Neish, loc.cit.) has been shown to give 3-carbethoxy-5:6,3':2'-indenodioxindole, I, and not 3-carbethoxy-4:5.2':3'-indenodioxindole, II, for, by suitable degradations, fluorene-3-carboxylic acid, VI, and not fluorene-1-carboxylic acid, VII, was obtained. Studies leading to the alternative synthesis of fluorene-3-carboxylic acid are described.

The reaction of oxomalonic ester with primary aromatic amines gives compounds of general structure III (Martinet et al., Bull. Soc. 1922, 31, 435; Compt. rend. 1921, 172, 220; ibid. 1918, 166, 851 and 998; ibid. 1913, 156, 1625; Ann. Chim. 1915, 11, 85).

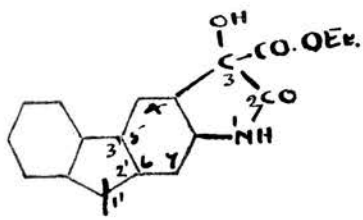


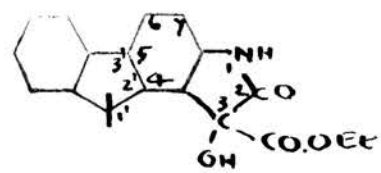
III

Such compounds are, in this thesis, referred to, for nomenclature purposes, as derivatives of the ketonic tautomeric form of dioxindole, B.

A B

In the case of 2-aminofluorene two possible structures exist for the product of such a reaction namely I and II.



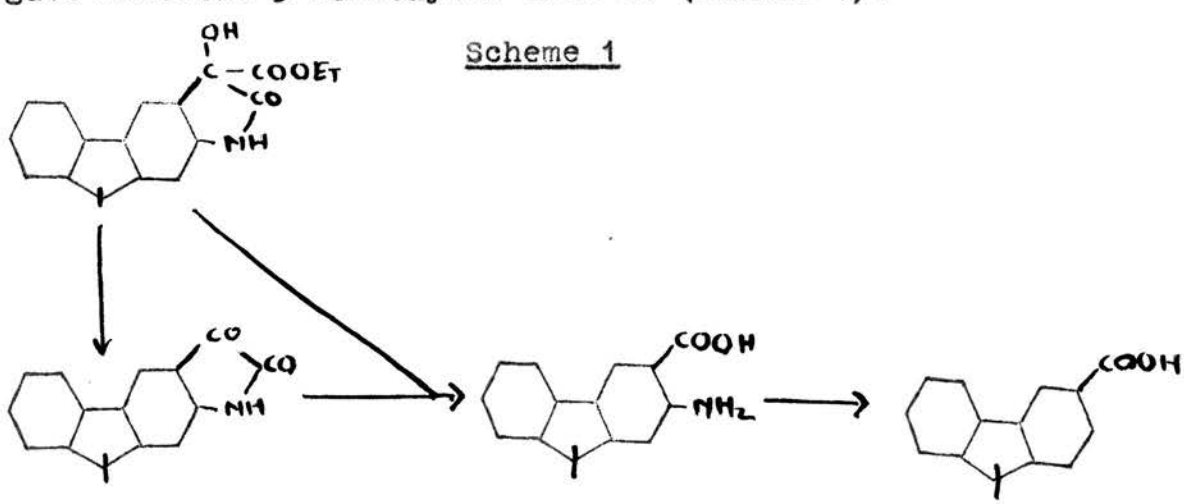


I. 3-carbethoxy-5:6, 3':2'-indenodioxindole

II. 3-carbethoxy-4:5, 2':3'-indenodioxindole

The product isolated by Neish had in fact the structure I for on oxidation it yielded the indeno-anthranilic acid, V (2-aminofluorene-3-carboxylic acid), which on deamination gave fluorene-3-carboxylic acid VI (Scheme 1).

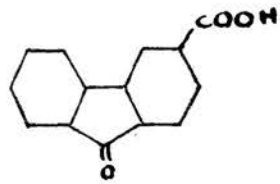
Scheme 1



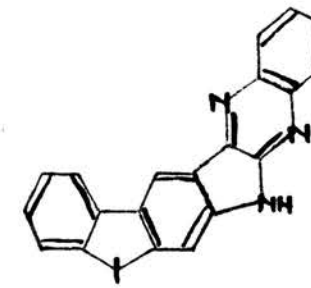
IV V m.p. 251-2°C VI mp. 231°C.

The indenoisatin, IV, corresponding to I was made by Neish's method; the aeration of the alkaline solution of I followed by acidification yielded, IV, but before acidification crystals were observed to separate. These were filtered off and examined, but no interpretable analysis could be obtained; the compound appears to be related to the sodium salt of 2-aminofluorene-3-glyoxalic acid. The indenoisatin, IV, and the 3-carbethoxy indenodioxindole, I, both gave on treatment with alkaline peroxide 2-aminofluorene-3-carboxylic acid V. This was deaminated to fluorene-3-carboxylic acid VI (m.p. 231°C) which had not previously been described in the literature. A mixed melting point with authentic fluorene-1-carboxylic acid VII (m.p. 245°C) showed a depression (m.p. 210-15°C), but oxidation of the fluorene-3-carboxylic acid gave a fluorenone-carboxylic acid, m.p. 300-1°C and fluorenone-3-carboxylic acid VIII has been described as possessing m.p. 285°C (Sieglitz & Schatzkes, Ber. 1921, 54, 2070; Kruber, Ber. 1932, 65, 1382). This discrepancy together with the fact that fluorene-3-carboxylic acid was unknown instigated attempted syntheses of fluorene and fluorenone-3-carboxylic acids (see page).

The indenoisatin IV was characterised as its 2:4-dinitrophenylhydrazone and as the quinoxaline derivative IX.



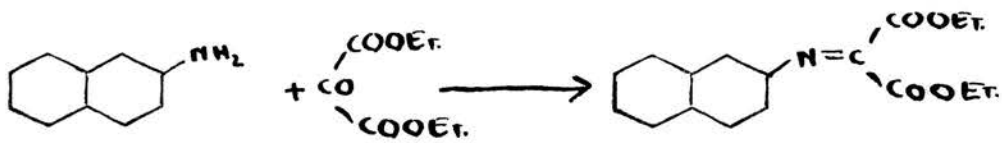
VIII



IX

In view of Caronna's (loc.cit.) degradation of isatin to anthranilamide (yield unspecified) it was at one stage thought advantageous to investigate the possible production of the indenoanthranilamide from I and IV by the Schmidt procedure. Repetition of Caronna's work gave a 40% yield of pure anthranilamide but I and IV only gave an intractable sulphur containing complex. This was soluble in aqueous acetone and was precipitated by ether but could not be obtained pure. Neither alkaline digestion nor acid treatment yielded a pure substance. In an effort to discover the reason for this failure, fluorene, was treated under the Schmidt reaction conditions. Amination to 2:7-diaminofluorene (10%) occurred together with the formation of a coloured intractable complex. These reactions may also be occurring with I and IV.

Throughout this work model reactions were carried out in the naphthalene series. From the reaction of β-naphthylamine and oxomalonic ester an intermediate was isolated whose analysis was compatible with structure X.



X

On aeration of X in alkaline solution followed by acidification the expected benzoisatin was obtained.

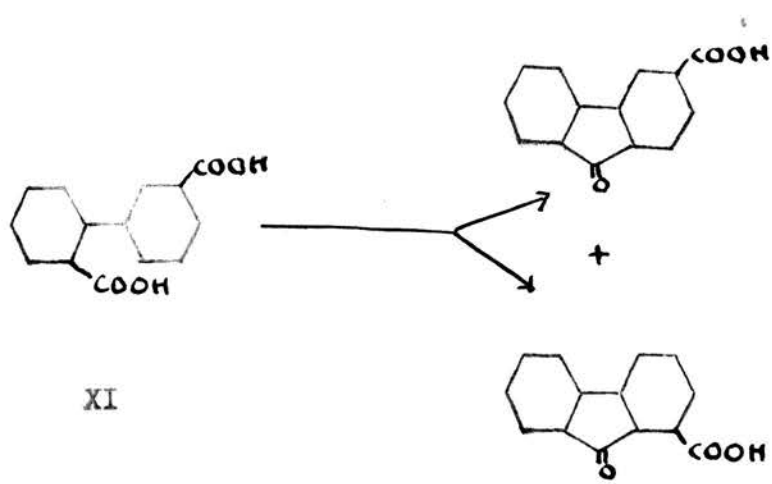
In another approach to the problem the synthesis of 2-aminofluorene-1-carboxylic acid from 2-nitrofluorenone-1-carboxylic acid (page) was contemplated. This, by comparison with V, should indicate the orientation of the condensation product. Before the oxidation of 4-nitrofluoranthene was attempted, model experiments were begun on the products of nitration of fluorenone-1-carboxylic acid. In addition to the known 7-nitrofluorenone-1-carboxylic acid, a dinitrofluorenone-1-carboxylic acid was obtained. These experiments were subsequently discontinued when fluorene and fluorenone-3-carboxylic acids were synthesised.

The sodium salt related to 2-aminofluorene-3-glyoxalic acid was also partially examined. The analyses were in agreement with the formula $C_{15}H_{10}NNaO_x$ where x was nearly seven rather than three. It was difficult to interpret this but in its reactions the compound had the properties expected of the sodium salt of 2-aminofluorene-3-glyoxalic

acid. On acidification to pH 6 with cold IN hydrochloric acid, an acid was deposited which on dissolving in excess acid could be diazotised and coupled with β-naphthol. Heating in attempted recrystallisations or treatment with more concentrated acids gave the indenoisatin. An attempted deamination of the acid using ethanol as reducing agent for the diazonium compound gave an acidic substance possessing ketonic properties. It was found impossible, however, to isolate any quantity of pure fluorene-3-glyoxalic acid.

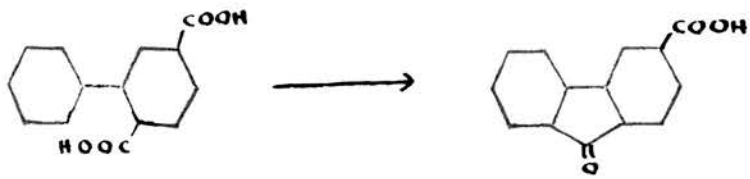
The synthesis of fluorene and fluorenone-3-carboxylic acids

The methods that seemed most possible were (1) by the cyclisation of 2:3'-diphenyldicarboxylic acid XI followed by separation of the mixture of fluorenone-1-carboxylic acid and fluorenone-3-carboxylic acid.



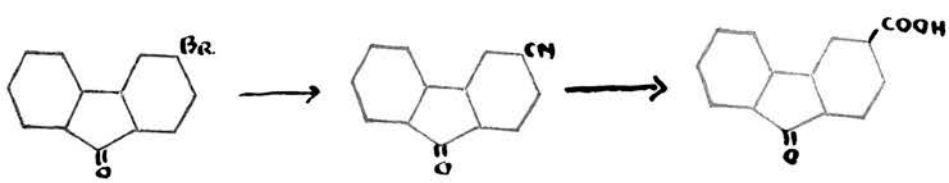
XI

(2) By the cyclisation of 3-phenylterephthalic acid XII.



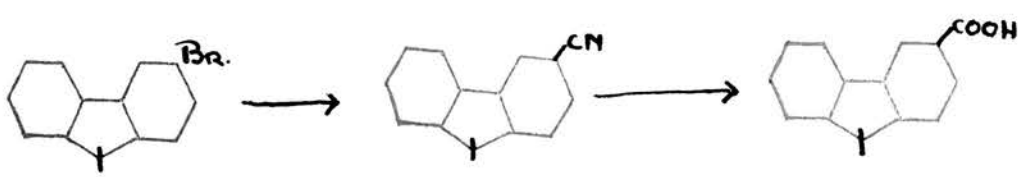
XII

(3) From 3-bromofluorenone, XIII, or 3-bromofluorene, XIV, by replacement of halogen by a cyano-group.



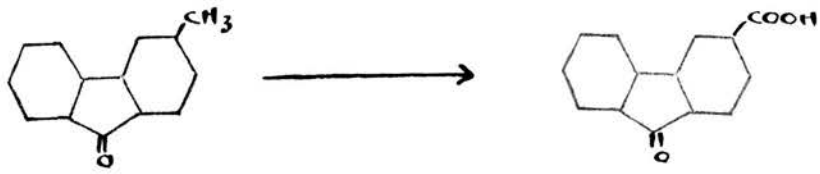
XIII

or



XIV

(4) From 3-methylfluorenone, XV, by oxidation of the methyl group.



XV

The latter was the original method employed by Sieglitz and Schatzkes and, as the purpose of the new work was to account for a melting point discrepancy, it was decided that a method quite different from that employed for the preparation of the two samples should be established. Method 1 was found to give reasonable results. Methods (2) and (3) were both partially examined but were eventually abandoned when (1) proved successfull.

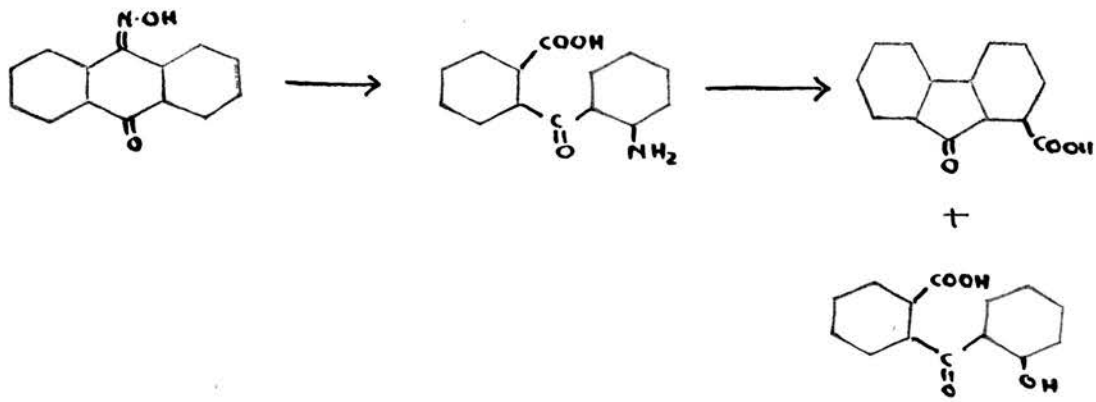
Method 1. The required isodiphenic acid, XI, had been prepared in two ways (a) by the oxidation of 2:3'-dimethylbiphenyl (Mayer & Freitag, loc. cit.) (b) by the alkaline fusion of fluorenone-1-carboxylic acid (Fittig and Liepmann, loc.cit.). Method (b) was employed using the conditions of Huntress and Seikel (J.A.C.S., 1939, 61, 1358). The cyclisation of XI was one of the first methods used for the synthesis of fluorenone-1-carboxylic acid (page 95. Mayer

& Freitag, loc.cit.) but the low yield,12%,was not explained and must be due to the difficulty of separating the fluorenone-1-carboxylic acid from the fluorenone-3-carboxylic acid simultaneously formed. That this was the case was clearly shown by repetition of the cyclisation when the two components of the reaction product mixture were only separated with low efficiency and with considerable trouble. The fluorenone-3-carboxylic acid was finally obtained, after hydrolysis of its methyl ester, as slender yellow needles, m.p. 304°C. A mixed melting point with the product of oxidation of the fluorene-3-carboxylic acid obtained from I showed no depression. Clemmenson reduction of the fluorenone-3-carboxylic acid gave fluorene-3-carboxylic acid identical with that obtained in the degradation of I.

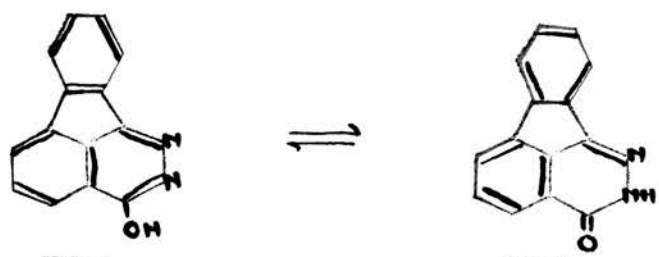
The validity of any conclusions based on this synthesis is limited by any possible doubt regarding the orientation of fluorenone-1-carboxylic acid. The structure of fluoranthene, which was established on the basis of the isolation of fluorenone-1-carboxylic acid by oxidation, has been adequetely confirmed by other methods. No structure could be contemplated on the basis of fluorenone-3-carboxylic acid as its oxidation product. In addition fluorenone-1-carboxylic acid has been unequivocally synthesised by several groups of workers. (Sieglitz, Ber. 1924, 57, 316; Butterworth,Heilbron, Hey and Wilkinson, J. 1938, 1386-9;

Lothrop and Goodwin, J.A.C.S. 1943, 65, 363-7). Sieglitz method is illustrated in Scheme 2.

Scheme 2



A neat demonstration of the structure of fluorenone-1-carboxylic acid was given by condensing it with hydrazine hydrate to give a cyclic hydrazone/hydrazide XVI B.



XVIA XVIB

This compound is considered for nomenclature purposes as a derivative of 1:2-diazofluoranthene, namely 3-hydroxy-1:2-diazofluoranthene- the ketonic tautomeric form. The formation of XVIB must be a complicating feature of the Wolff-Kishner reduction of fluorenone-1-carboxylic acid, as it is fairly stable to alkali.

The discrepancy between the melting points of the fluorenone-3-carboxylic acid quoted by Kruber, and by Sieglitz and Schatzkes and that found here must now be discussed (Table I).

Table I

Sieglitz and Schatzkes	m.p. 285-6°C	yellow crystalline "pimples"
Kruber	m.p. 283-4°C	yellow plates
From ester	m.p. 304°C	slender yellow needles
From fluorene-3-carboxylic acid	m.p. 301-2°C	" " "

Sieglitz and Schatzkes obtained their sample from the oxidation of pure 3-methylfluorenone but Kruber oxidised a mixed crystal of homologous methylfluorenes and separated the resulting methylfluorenones and fluorenone carboxylic acids to obtain his product. The difficulties experienced by Kruber in his separation must have been greater than those described in the experimental section (page) and he makes no mention of purification via the ester which was found necessary. Crystallisation alone gave a product which formed little hard nodules (cf. pimples) which were patently impure. The product of Sieglitz and Schatzkes cannot be disposed of so readily but if it was not impure then the possibility of dimorphism cannot be ignored.

Method 2. The synthesis of 2-phenylterephthalic acid was attempted by a Gomberg reaction using 2-amino-dimethylterephthalate in a manner analogous to the synthesis of 3-phenylphthalic acid by Butterworth, Hey, Heilbron, and Wilkinson (loc.cit.), (Scheme 3).

Scheme 3

In the synthesis of 2-amino-dimethylterephthalate only one innovation was introduced. The nitration of terephthalic acid was carried out with potassium nitrate in concentrated sulphuric acid. The attempts to carry out the Gomberg reaction were uniformly unsuccessful.

Method 3. This work will be discussed as follows:

(a) The synthesis of 3-bromofluorenone by the method of Miller and Bachman.

(b) The synthesis of 3-aminofluorene.

(c) The mercuration of fluorene.

(a)

The method of Miller and Bachman (loc.cit.) consists essentially in the formation of 2-(4'-bromobenzoyl)-aniline by the Hofmann degradation of the 2-(4'-bromobenzoyl)-benzamide. They claimed high yields at every stage. Repetition of their work showed many glaring discrepancies. Their results and those found on repetition are summarized in Table 2 below.

Table 2

Compound	m.p. (pure)	Yield (pure)	m.p.(M&B)	Yield(M&B)
2-(4'-bromo-benzoyl)-banzamide	224°C	66% (+30% impure)	184-184·5°C	95%
2-(4'-bromo-benzoyl)-aniline	112°C (Picrate m.p.136°C)	20%	107-108°C (uncharacterised)	82·5%
3-bromo-fluorenone	168°C	40-50%	163°	92%

The most obvious variation is in the melting point of the substituted benzamide and in the yields of the substituted aniline and the 3-bromofluorenone. Huntress, Pfister and Pfister (loc.cit.) found very similar deviations when they repeated the work of Miller and Bachman on the preparation of a 2-benzoyl bromobenzamide and its conversion to a bromofluorenone. Here there were even more serious

implications as Miller and Bachman had used two unequivocal syntheses to obtain the bromoflorenone and in both cases they obtained identical products but subsequent work has shown that the structure assigned to the 2-benzoyl bromobenzamide used by Miller and Bachman was wrong. The two syntheses could not therefore have given the same bromofluorenone. In addition to this the 4 possible bromofluorenones have all now been synthesised. Huntress Pfister and Pfister pointed out that the physical characteristics found by Miller and Bachman for they product in no way agree with those for any of the bromofluorenones. The work of Miller and Bachman must therefore be treated with reserve especially as their analyses at two critical points are unsatisfactory.

(1) In the analysis of their amide only the value for bromine was given; where an amide has been produced from an acid the only truly indicative analytical data is the nitrogen value as $-NH_2$ replacing OH reduced the molecular weight by only 1.

(2) No analysis for the product of the Hofmann degradation was given. The only analysis given for 2-(4'-bromobenzoyl)-aniline is for a product isolated in 2% yield from an Oesterlin reaction on 2-(4'-bromobenzoyl)-benzoic acid.

(b)

The synthesis of 3-nitro-2-aminofluorene was carried out by the classical method of Diels (page 44). Only a

few minor variations, described in the experimental section were introduced. The attempted deamination of 3-nitro-2-aminofluorene by the method of Hayashi and Nakayama (loc.cit.) failed. The reaction gave mainly a red product; this was more in line with the findings of Diels who deaminated 7-nitro-2-aminofluorene in relatively poor yield obtaining a red material as the principal product. The method of Hodgson and Walker (J. 1933, 1620) was used with equally poor results. Eventually 3-aminofluorene was obtained by reduction of 2-bromo-3-nitrofluorene with stannous chloride (cf. Sandin and Evans, loc.cit.). The 2-bromo-3-nitrofluorene was obtained from 2-amino-3-nitrofluorene by an amendment of the method of Campbell Anderson & Gilmore (J. 1940, 446). It was found that the addition of a glacial acetic acid solution of the amine to potassium nitrite in conc. sulphuric acid caused too great an evolution of heat due to the dilution of the sulphuric acid. An equal volume of acetic acid was therefore added to the sulphuric acid and this was cooled before adding the 2-bromo-3-aminofluorene. Campbell Anderson & Gilmore described the 2-bromo-3-aminofluorene as a red compound; it is in fact a pale straw coloured compound.

The attempted passage to 3-bromofluorene from 3-aminofluorene gave only poor results and as the object of the work had by then been achieved, the examination of

the reaction conditions was discontinued.

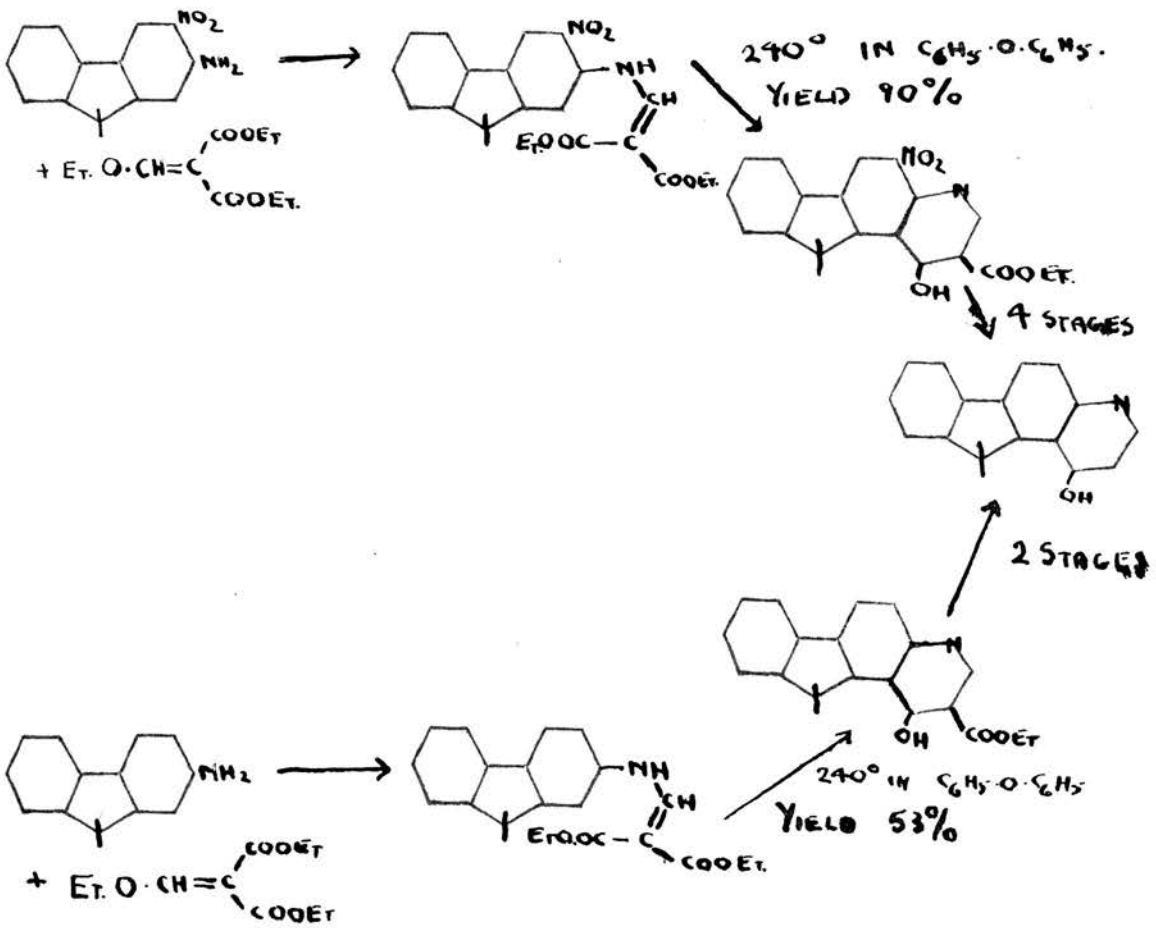
(c)

Miller and Bachman (loc.cit., see page 31 et seq.) carried out the mercuration of fluorene by two procedures and they converted the mercurichlorides thus obtained into bromofluorenes by treatment with bromine in acetic acid. Their claims to have obtained two monobromofluorenes in the course of these studies have been investigated, especially as they claim that one of these compounds was 3-bromofluorene, m.p. 90-94°C, yielding 3-bromofluorenone on oxidation. Repetitions of their work showed that no monobromofluorenes were in fact produced but, that, apart from bromomercuri fluorenes, only dibromofluorenes and a little fluorene were in fact obtained. Their compound melting point 90-94°C which they claim to be identical with one obtained by reduction of 3-bromofluorenone, m.p. 94°C, is probably a mixture of fluorene and bromofluorenes. They make the singular claim to have isolated a monobromocompound, m.p. 163°C, which in fact contains two atoms of bromine per molecule. On oxidation it yielded a dibromofluorenone, m.p. 139.5°C, and this should be compared with the monobromofluorenone claimed to be formed by Miller and Bachman, m.p. 183°C. As all the monobromofluorenones are now known and as the highest melting point obtained for

any of them is 163°C for 3-bromofluorenone, added cogency is given to the questionable nature of the work of Miller and Bachman.

The theoretical aspects of this work. The theoretical basis of this work has been fully discussed in Part I. Since it was written Bremer and Hamilton (J.A.C.S. 1951, 73, 1844) have published work which is in apparent contradiction to many of the statements made. Their work is schematically shown below.

Scheme 4



From this it might be deduced that syntheses such as the Skraup etc. might also go in the 1-position but the evidence from the oxomalonic ester condensation is equally strongly in favour of the 3-position. The principal differences are that, whereas the oxomalonic ester condensation was carried out at a 120°, the above cyclisation occurred at 240°C. The disparity in yield between the 3 substituted and 3 unsubstituted 2-aminofluorene is perhaps significant also. The conclusion from the combination of the above and the work reported in this section is that all the theoretical analyses must be done with extreme care. In the picture of the fluorene molecule conceived in Part I, the difference between positions 1 and 3 were regarded as small but sufficient to discriminate in favour of 3. This difference might disappear and the discrimination might be reversed by a temperature factor. Generalisations should not therefore be made regarding the reactions of 2-aminofluorene on the basis of the meagre and contradictory evidence available. The conclusion that the Skraup reaction almost certainly yielded 6:7,3':2'-indenoquinoline, based on the absorption spectra (page 50), should now be regarded as perhaps slightly less convincing.

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249. *The Oxidation of* 4 : 11-*Dibromofluoranthene.*

By Neil Campbell, W. H. Stafford, and J. F. K. Wilshire.

It was shown (Campbell, Easton, Rayment, and Wilshire, *J.*, 1950, 2784) that chromic acid oxidation of dibromofluoranthene yields 2 : 7-dibromofluorenone-1-carboxylic acid and a monobromo-acid provisionally regarded as 6-bromofluorenone-1-carboxylic acid (II). We have now

(I.) (II.)

confirmed this formulation by decarboxylation of the acid to 3-bromofluorenone, showing that the acid (II) is formed by oxidation of the ring A (I) and providing further evidence that the original compound is 4 : 11-dibromofluoranthene (cf. Holbro and Tagmann, *Helv. Chim. Acta*, 1950, **33**, 2178).

Experimental.—The mixture of acids obtained by oxidation of dibromofluoranthene was boiled with successive 500-ml. portions of calcium hydroxide solution and the hot solutions were filtered. The cold filtrates deposited the calcium salt of the dibromo-acid and the filtrate on acidification gave 6-bromofluorenone-1-carboxylic acid, which crystallised in yellow rosettes, m. p. 253—255°, from glacial acetic acid and gave a *methyl* ester, m. p. 126—127° (Found: Br, 25·8. $C_{15}H_9O_3Br$ requires Br, 25·2%). The acid on decarboxylation with quinoline and copper-bronze afforded 3-bromofluorenone, yellow leaflets (from light petroleum), m. p. 162—163°, undepressed on admixture with an authentic sample Found: Br, 31·2. Calc. for $C_{13}H_7OBr$: Br, 30·9%). This substance was prepared from *o*-(4-bromobenzoyl)benzamide by Miller and Bachman's method (*J. Amer. Chem. Soc.*, 1935, **57**, 2443), but we were unable to attain the high yields reported by them. By adding a benzene solution of the acid chloride to saturated methanolic ammonia we prepared the substituted benzamide, and after repeated crystallisation from xylene, xylene–acetone, and acetic acid obtained it as needles, m. p. 224° (Found: N, 4·4; Br, 24·1. Calc. for $C_{13}H_{10}O_2NBr$: N, 4·6; Br, 26·3%). The substance is clearly not quite pure (probably owing to adhering solvent), but nevertheless it melts nearly 40° higher than Miller and Bachman's product (m. p. 184·5—185°), which we think was a mixture of acid and amide. The amide was converted *via* 2-amino-4′-bromobenzophenone, m. p. 112°, into 3-bromofluorenone, which had the m. p. given by other workers (*e.g.*, Heilbron, Hey, and Wilkinson, *J.*, 1938, 113).

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Experimental

2-Nitrofluorene. The method of Diels (Ber., 1901, 34, 1758) was found to give consistent results. Benzene was preferred to glacial acetic acid for crystallisation. Yield 80-85%, m.p. 157°C.

The method of Calderon and Cerrato (British Abstracts, 1949, p. 75) was attempted but found to be unsatisfactory. The conditions employed are given below and should be accepted only as an interpretation of the rather brief abstract.

Fluorene (25 gms.) was stirred into nitric acid (100mls. D.1.4) at 15°C to give an even suspension. The temperature was carefully raised to 20°C when a change in colour of the suspended solid from white to yellow occurred with simultaneous warming. External cooling was used to maintain the temperature at 20-25°C. After 10 minutes the temperature fell to 15°C and the yellow sludge was transferred to a mechanical shaker in which it was vigorously agitated for 30 minutes. The temperature did not rise during this process and the sludge was finally ground thoroughly in a mortar. On pouring into water (500 mls.) yellow 2-nitrofluorene was deposited. After filtration and air drying the solid was dried by azeotropic distillation with benzene. The 2-nitrofluorene (29 gms.) obtained by crystallisation from

benzene solution was of poor appearance and melting point (m.p. 148-50°C). Fractional crystallisation from (1) benzene (2) glacial acetic acid (3) alcohol in that order eventually gave 10 gms. m.p. 153-4°C together with other less pure fractions. It was concluded that the method is not suitable for preparing pure 2-nitrofluorene; the colour suggests the presence of di- and poly-nitrofluorenes and this was confirmed by a later observation (see below.) Fluorene was absent.

2-aminofluorene. The classic method of Diels (loc.cit.) was extremely reliable and modifications e.g. that of Sampey and Reid (J.A.C.S. 1947, 69, 712) were found to be unsatisfactory due to 2,2'-azoxybisfluorene formation (cf. Cislak, Eastman and Senior, J.A.C.S. 1927, 49, 2318). The reduction of 2-nitrofluorene with iron filings in hydrochloric acid containing 50% ethanol gave quite good results but was not equal to the method of Diels.

To 2-nitrofluorene (25 gms.), ironfilings (50 gms.) a mixture of ethanol (100 mls.) and conc. hydrochloric acid (25 mls.) was added. The mixture was boiled for four hours and every 15 minutes during the first two hours further additions of conc. hydrochloric acid (15 mls.) were made. The hot solution was eventually filtered to remove excess ironfilings; the filtrate which was almost neutral was poured into water (300 mls.) containing sodium acetate

(25 gms.). The 2-aminofluorene precipitated was removed by filtration and dried (15 gms., m.p. 123-5°C). Recrystallisation from 50% aqueous ethanol or petrol ether/ethyl acetate gave 2-aminofluorene (12 gms., m.p. 127°C).

2-Nitrofluorene (m.p. 149-151°C) made by the method of Caldèron and Cerrato when used in this reaction gave a blue colour on filtration of the hot solution after the reduction. This is probably due to the aeration of the ferrous chloride solution which contains some 2:5- and 2:7-diaminofluorene.

3-Carbethoxy-5:6,3':2'-indenodioxindole. Neish (loc.cit.) does not state the yield in the preparation of this compound. Repetition of his work, showed that the yield, under apparently identical conditions, was very variable.

2-Aminofluorene (15 gms.) in acetic acid (125 mls.) was added to oxomalonic ester (15 gms. Organic Syntheses, Vol. I, 267) in acetic acid (125 mls.) and the mixture was boiled under reflux for 2 hours. Charcoal (2 gms.) was added and boiling was continued for a further 15 mins. The solution was hot-filtered and set aside for 24 hours when the buff coloured crystals were removed by filtration and recrystallised from glacial acetic acid. Yield 11-14 gms., m.p. 247-9°C. Attempts to obtain a further quantity from the original mother liquors was unsuccessful.

2-Aminofluorene-3-carboxylic acid. To 3-carbethoxy-5:6,3':2'-indenodioxindole (0.25 gms.) dissolved in alcohol (5 mls.) containing 4N aqueous caustic soda solution (5 mls.) was added perhydrol (2 mls.). The colour was rapidly dispelled. Gentle warming was applied until the evolution of oxygen ceased; the solution was then diluted with water (50 mls.) containing sufficient acetic acid to make the solution slightly acid. The precipitated amino acid was thoroughly extracted in ether (4 x 25 mls.) and the combined fluorescent ether layers were concentrated (c. 15 mls.), after drying over sodium sulphate. Dry hydrogen chloride was passed through the ethereal solution to give the aminoacid hydrochloride which was isolated by decantation of the supernatant solution and washing with ether. After the residual ether had evaporated from the buff-coloured solid in the reaction flask, the hydrochloride was taken up in water (5 mls.) and was decomposed with saturated sodium acetate solution. The amino acid was filtered off and, after drying, was recrystallised from glacial acetic acid. Yield 0.12 gms., mp. 251-2°C (dec.). Further crystallisation (charcoal) of the gleaming plates removed the brown colour and the melting point was raised to 256°C but the yield was seriously reduced.

$C_{19}H_{11}NO_2$ requires 74.7%C, 4.9%H, 6.2%N.

Found 74.3%C, 4.3%H, 6.3%N.

Fluorene-3-carboxylic acid. The reduction of the diazonium chloride derived from 2-amino-fluorene-3-carboxylic acid was carried out both with ethanol and with hypophosphorous acid. The latter gave better results.

2-Aminofluorene-3-carboxylic acid (0.1 gms.) was dissolved in hydrochloric acid (2 mls. conc. hydrochloric acid in 2 mls. water) with warming. After cooling to 0°C a slight excess of saturated sodium nitrite solution was added with stirring. The temperature was now allowed to rise to 10°C over a period of 10 minutes when a previously prepared solution of calcium hypophosphite (2 gms.) in hydrochloric acid (4 mls. conc. hydrochloric acid in 4 mls. ethanol) was added. After two hours the temperature was raised over a period of 30 minutes to 85°C. Nitrogen was initially evolved but after 30 minutes at 85°C reaction had ceased. The solution was poured into water (50 mls.) and the solution was filtered. The filtrate was extracted with ether (2x25 mls.) and the filtered and washed solid was taken up in this ethereal extract. After drying over sodium sulphate the ether was removed and the buff solid was recrystallised from glacial acetic acid (charcoal). Scintillating rhombic prisms (0.042 gms., m.p. 231°C) were obtained which were very pale yellow but which after sublimation, were white.

$C_{14}H_{10}O_2$ requires 80.0%C, 4.8%H.

Found 79.2%C, 4.8%H.

Fluorenone-3-carboxylic acid. Fluorene-3-carboxylic acid (0.05 gms.) in 4N caustic soda solution (2 mls.) was oxidised with finely powdered potassium permanganate (0.2gms.). After heating at 100°C for 1 hour the solution was acidified with dilute hydrochloric acid containing sufficient sodium bisulphite to decolourise the solution and dissolve the manganese dioxide. The cooled solution was filtered, and the pale yellow solid resulting was recrystallised from glacial acetic acid (charcoal). Fluorenone-3-carboxylic acid (0.02 gms., m.p. 300-1°C), was obtained as tiny yellow needles. Mixed m.p. with fluorenone-3-carboxylic acid, synthesised as below, showed no depression.

5:6,3':2'-Indenoisatin. The method of Neish (loc.cit.) gave excellent results. It was found however that when the aeration of the alkaline solution of the carbethoxy compound was nearing completion, a solid separated. The addition of alcohol and cooling of the solution gave a good yield of a salt which appears to be the sodium salt of 2-aminofluorene-3-glyoxalic acid but the analyses were unsatisfactory. The ratios of C:N:H:Na was compatible with the formula $C_{15}H_{10}N\ Na\ O_x$ but x was apparently much larger than the required value of 3. Treatment of the sodium salt with ice-cold IN hydrochloric acid gave a light coloured acid but any attempts to recrystallise it gave the indenoisatin. Treatment of the sodium salt with concentrated hydrochloric acid also gave the indenoisatin.

Quinoxaline derivative of 5:6,3':2'-indenoisatin. Treatment of the indenoisatin in alcohol solution with O-phenylenediamine in the usual manner gave the quinoxaline derivative

$C_{21}H_{13}N_3$ requires 13.7%N, 82.1%C, 4.2%H.

Found 13.5%N, 81.6%C, 3.5%H.

The compound crystallised from acetic acid as lemon yellow needles with a melting point greater than 360°C. Sublimation and decomposition occurred after 340°C.

The Oxidation of 5:6,3':2'-indenoisatin. The oxidation of 5:6, 3':2'-indenoisatin with alkaline peroxide in a manner identical with that previously employed for 3-carbethoxy-5:6,3':2'-indenodioxindole gave 2-amino-3-fluorene carboxylic acid.

The Schmidt reaction of isatin. The conditions employed were those of Caronna (Gazz., 1941, 71, 585). The yield of anthranilamide, m.p. 108°C, was 40% of theoretical.

The Schmidt Reaction of 5:6,3':2'-indenoisatin and 3-carbethoxyindenodioxindole

When the reaction was carried out in a manner identical with that of Caronna an insoluble sulphur containing compound was obtained from both the isatin and the carbethoxydioxindole. This proved highly intractable and no pure product was isolated. The use of trichloracetic acid in place of sulphuric acid as a solvent for the reaction of the carbethoxydioxindole gave a good return of starting

material. In trichloracetic acid solution the 3-carbethoxy-5:5-3':2'-dioxindole gives a deep blue colour.

The Reaction of Fluorene and Hydrazoic Acid

Fluorene (5 gms.) was suspended in conc. sulphuric acid (12 c.c.). Sodium azide (5 gms.) was added in five portions at five minute intervals while vigorous stirring was continued; the temperature was kept below 25°C during the reaction period (2 hours). On pouring into water (100 mls.) and filtering, a greenish mass was removed. This proved to be unchanged fluorene (4 gms.) and a greenish complex of unknown nature (0.5 gms.). The acid filtrate was made alkaline and was then extracted with ether (3x100 mls.). The combined ether layers were dried over sodium sulphate and then the ether was removed. Recrystallisation of the residual material from aqueous ethanol and the petroleum ether gave impure 2:7-diaminofluorene (0.15 gms.). The diacetyl derivative was prepared and although the amine and the derivative both melted 2° below the quoted values, mixed melting points with authentic material showed no depression. The colour reactions, e.g. with chlorine water or blood, so characteristic of benzidine derivation were given.

2:3'-Diphenyl dicarboxylic acid, cf. Huntress and Seibel (J.A.C.S., 1939, 61, 1358).

Caustic potash (30 gms.) was added to diphenyl ether (125 mls.) and the mixture was vigorously stirred while the temperature was raised to 200°C (bath temperature 230°C).

To the resulting emulsion powdered fluorenone-1-carboxylic acid (10 gms.) was added portionwise. The additions were complete after 5 minutes but the vigorous stirring was continued for 10 minutes more when heating and stirring were both stopped. After cooling, the reaction mixture was poured into water (100 mls.) and the flask was rinsed with more water (50 mls.). The solidified diphenyl ether presented several mechanical difficulties at this stage, so carbon tetrachloride (150 mls.) was added to dissolve the ether. The aqueous layer was separated and was washed with carbon tetrachloride (50 mls.) before being acidified, cooled, and filtered. The resulting solid contains unchanged fluorenone-1-carboxylic acid, 2:3'-diphenyl dicarboxylic acid and a coloured contaminant requiring charcoal screening for its removal.

The solid was extracted with boiling water (1 litre) for 5 minutes and the undissolved material was separated by hot filtration. The filtrate was now treated with charcoal (2 gms.) for 5 minutes at 100°C. After filtration and cooling white fluffy clumps of elongated prisms were deposited. These were separated by filtration. The filtrate was now used to re-extract the residue undissolved in the primary extraction. This cycle was continued until no further extraction occurred. The residue was fluorenone-1-carboxylic acid and was recrystallised from ethanol. The crystalline mat obtained from the aqueous extract was

recrystallised from aqueous methanol or benzene/ethanol and was 2:3'-diphenyl dicarboxylic acid, m.p. 216-7°C.

$C_{14}H_{10}O_4$ requires 69.4%C and 4.17%H.

Found 69.6%C and 4.15%H.

The yield was variable but was never less than 5 gms. (Theoretical 10.3 gms.). The recovery of fluorenone-1-carboxylic acid, however, made the overall yield 75-80%. The other isomer, 2:3-diphenyl dicarboxylic acid did not appear to be present in any appreciable quantity. The other 20% is apparently to be explained by the presence of brown material removed by the screening and by the presence in the diphenyl ether of some non-acidic material.

The dimethyl ester was prepared by the action of diazomethane in ether in the normal way. 0.45 mgs. acid gave 0.40 gms. pure ester, m.p. 71-2°C. This crystallised from petrol-ether (b.p. 40-60°C) in lozenges.

$C_{16}H_{14}O_4$ requires 71.1%C and 5.2%H.

Found 71.3%C and 5.2%H.

Fluorenone-3-carboxylic acid. 2:3'-diphenyl dicarboxylic acid (2.5 gms.) was dissolved in conc. sulphuric acid (25 mls.) by warming to 140°C at which temperature it was maintainedfor one minute. The deep red solution was now treated in two ways in different series of experiments.

(1) The solution was poured into water (100 mls.) and this was boiled and the suspension of yellow solid was filtered hot. The solid was washed with boiling water and the filtrate deposited a little starting material on cooling. The yellow residue was dissolved in boiling alcohol (300 mls.). On standing a yellow precipitate was deposited followed by a little orange fluorenone-1-carboxylic acid. The solid (c. 1.3 gms.) was filterd off and was heated with alcohol (50 mls.) at the boiling point for 10 minutes. About one third to one half dissolved, the undissolved portion being substantially pure fluorenone-3-carboxylic acid. Complete purification can only be effected by esterification and hydrolysis of the ester.

Crude fluorenone-3-carboxylic acid (0.5 gms.) was dissolved in methanol (20 mls.) containing conc. sulphuric acid (2 mls.). The solution was boiled under reflux for one hour and was then poured into water (50 mls.). Extraction with ether (4x50 mls.) gave a yellow ethereal solution of the ester which, after drying over anhydrous sodium sulphate, was distilled to remove the ether. The ester was recrystallised from methanol and petrol-ether, and had a m.p. 145°C. The yield of slender pale yellow needles was 0.4 gms.

$C_{15}H_{10}O_3$ requires 75.6%C and 4.2%H,

Found 75.4%C and 4.3%H.

Fluorenone-3-carboxylic acid methyl ester (0.2 gms.) was dissolved in alcohol (4 mls.). Aqueous caustic soda solution (1 ml., 30%) was added and the mixture was boiled for one hour, after which it was poured into water (10 mls.). The solution was extracted with ether (15 mls.) and the aqueous layer was then acidified. The precipitated fluorenone-3-carboxylic acid was recrystallised from glacial acetic acid forming slender yellow needles (0.17 gms., m.p. 304°C).

Required 75.0%C and 3.7%H.

Found 74.8%C and 3.6%H.

(2) The red solution was poured into methanol (200 mls.) and the solution was boiled for 2 hours. The methanol solution was concentrated to 100 mls. and was poured into water (200 mls.). Extraction with ether (5x100 mls.) was followed by drying over sodium sulphate and distillation of the ether. The crude mixture of methyl esters of fluorenone-1-carboxylic acid and fluorenone-3-carboxylic acid (2.5 gms.) was recrystallised from methanol. The slender yellow needles first deposited were almost pure fluorenone-3-carboxylic methyl ester (c. 0.5 gms.) but all subsequent fractions were mixtures of slender pale yellow needles and short thick prisms of a deeper yellow colour. In an effort to separate these compounds chromatography was employed. This resort, although thoroughly examined, was

not highly successful due to the combination of irreversible adsorption and the existence of a close similarity in the adsorption properties of the two esters. This latter required that alumina of high activity should be used in greater quantities than the usual ratio 30-50 gms. of alumina per 1 gm. of applied mixture. Acid treated alumina was not of sufficient activity to give good separation and normal Brockmann alumina only gave a 40-60% recovery of ester. Although small quantities of pure fluorenone-3-carboxylic acid methyl ester were thus obtained, the method is fraught with difficulties.

The fluorenone-3-carboxylic acid (m.p. 303°C) was obtained from the ester as before.

Fluorene-1-carboxylic acid and Fluorene-3-carboxylic acids. Both acids may be obtained by Clemmenson reduction of the corresponding ketoacids. Acetic acid and hydrochloric acid together were found to give unsatisfactory results due to the coating of the zinc with a yellow, insoluble gum during the reaction. The use of dioxan, acetic acid and hydrochloric acid gave good results.

The fluorenone acid (0.2gms.) was dissolved in a mixture of dioxan (5 mls.) and acetic acid (5 mls.). Conc. hydrochloric acid (2mls.) and a large excess of amalgamated granulated zinc, previously washed with acid, were now added and the

mixture was boiled under reflux with periodic additions of conc. hydrochloric acid (4x1 mls.) until the solution was colourless (2 hours). The solution was decanted from the zinc and was concentrated to 3-4 mls. before being diluted with water (20 mls.). After thorough cooling the deposited acid was filtered and recrystallised from glacial acetic acid (charcoal). Fluorene-1-carboxylic (0.17 gms., m.p. 245°) under these conditions crystallised as small rosettes of opaque white prisms. Fluorene-3-carboxylic acid (0.16 gms. m.p. 230°C) crystallised as scintillating rhombic prisms.

The condensation of Fluorenone-1-carboxylic acid and hydrazine

Fluorenone-1-carboxylic acid (0.20 gms.) in dioxan (5 mls.) containing hydrazine hydrate (1 ml. 90%) was heated at 100°C for 2 hours. The solid obtained on pouring into water was recrystallised from acetic acid yielding 1:2-diaza-3-hydroxy-fluoranthene (0.18 gms., m.p. 267-8°C).

$C_{14}H_8N_2O$ requires 76.4%C and 3.6%H.

Found 76.2%C and 3.5%H.

The nitration of fluorenone-1-carboxylic acid

Fluorenone-1-carboxylic (1 gm.) was dissolved in sulphuric acid (10 mls.) and finely powdered potassium nitrate (1 gm.) was added with stirring at room temperature. The mixture was then warmed in a water bath to 80°C for a short time when it was poured into water 100mls. The solid

precipitated was recrystallised from glacial acetic acid yielding what is probably 2:7-dinitrofluorenone-1-carboxylic acid (0.5 gms., m.p. 267°C).

$C_{14}H_6O_7N_2$ required 8.9%N.

Found 8.9%N.

β-naphthylamine and oxomalonic ester. An intermediate in the synthesis of 4:5-benzo-3-carbethoxydioxindole was obtained by the following procedure:

A mixture of β-naphthylamine (1 gm.) in glacial acetic acid (10 mls.) containing oxomalonic ester (1 gm.) was boiled for 1 hour under reflux; petrol ether (50 mls.) was now added together with sufficient benzene to prevent two liquid phases developing. Deposition ofprisms rapidly occurred. These were recrystallised from ethanol and gave the analysis 67.1%C and 5.2%H. On aeration of an alkaline solution followed by acidification 4:5-benzoisatin was obtained.

2-(4'-Bromobenzoyl)-benzamide. This was prepared from 2-(4'-bromobenzoyl)-benzoic acid (Ullmann and Sone, Ann. 1911, 380, 337) by the following method:

2-(4'-bromobenzoyl)-benzoic acid (30 gms.) was dissolved in thionyl chloride (50 gms.) and benzene (100 mls.) by boiling under reflux for 2 hours when the evolution of

hydrogen chloride had abated. By repeated co-distillation with benzene under reduced pressure the excess thionyl chloride was removed. The acid chloride dissolved in benzene to a volume of c. 120 mls. was added slowly to ethanol (250 mls.) saturated at 0°C with ammonia, while ammonia gas was bubbled vigorously through. The precipitated amide was filtered and, after washing with alcohol, it was thoroughly washed with warm water to remove ammonium salts. The resulting product (10-22 gms.) melted at 216-218°C, but this value was eventually raised to 224°C by recrystallisation from xylene, xylene/acetone, aqueous acetone and acetic acid, second fraction (8-10 gms.) obtained from the benzene/alcohol solution, had a melting point 200-206°C but was not susceptible to ready purification.

$C_{14}H_{10}O_2N$ Br requires 4.6%N and 26.3% Br

Found 4.4%N and 24.1% Br.

2-(4'-bromobenzoyl)-aniline. On using the conditions employed by Miller and Bachman (loc.cit.) very variable results were obtained. The crude product which they claimed to be substantially pure 2-(4'-bromobenzoyl)-aniline was extracted repeatedly with 50% hydrochloric acid until, on making alkaline, no yellow colour was produced or yellow solid deposited. The yellow amine was thoroughly extracted with ether (5 x 50 mls.) and after removing the ether the

compound was recrystallised from aqueous methanol then petroleum ether. It melted at 111°C and formed a picrate m.p. 136°C. The yield of amine is less than 20%.

$C_{13}H_{10}ONBr$ requires 28.9% Br.

Found 29.5% Br.

3-Bromofluorenone. Diazotisation of 2-(4'-bromobenzoyl)-aniline in the standard way followed by decomposition of the 2-(4'-bromobenzoyl)-benzene diazonium chloride by warming, yielded 3-bromofluorenone. After crystallisation from ethanol it melted at 163°C and was obtained in 45% yield. This should be contrasted with the high yield claimed by Miller and Bachman using the identical conditions on an impure amine.

2-Acetamidofluorene. On adding 2-aminofluorene (20 gms.) to a mixture of glacial acetic acid (50 mls.) and acetic anhydride (50 mls.) spontaneous warming occurred, the reaction was completed by heating on the steam bath for 15 minutes. Precipitation of the N-acetyl compound was completed by slow and circumspect addition of hot water (75 mls.). The solid mass obtained on cooling was filtered and, after removal of acetic acid by washing with water, the amide was dried first in the air and then by azeotropic distillation with benzene. The acetamido compound (185 gms.,

m.p. 192°C) crystallised on cooling its benzene solution and the mother liquors yielded a further 3 gms. of pure amide.

3-nitro-2-aminofluorene. The nitration of 2-acetamidofluorene yielded a mixture of the 3- and 7-nitro-2-acetamidofluorenes, which was hydrolysed to the free amines (Diels, Ber., 1902, 35, 3286). After a partial separation of the 3- and 7-nitro-2-aminofluorenes by virtue of their different basicities departure was made from the original method of Diels. The crude 3-nitro-2-aminofluorene was chromatographed on alumina (30 gms. per/gm. of crude product) with xylene (sulphur free) as developer and eluant. The crimson 3-nitro-2-aminofluorene band separated giving an orange yellow eluate which, after concentration, yielded exquisite crimson plates with a yellow sheen, m.p. 203°C. These on recrystallisation from acetic acid revert to the prisms described by Diels.

The Deamination of 2-amino-3-nitrofluorene. The deamination of this compound by the method of Hayashi and Nakayama (J.Soc.Chem.Ind. Japan, 1933, 36, 127B) even when modified by using the Hodgson Walker diazotisation method and using hypophosphorous acid for reduction of the diazonium sulphate did not give good yields of 3-nitrofluorene. The principal products was a red amorphous substance whose analysis was 61.7%C, 3.8%H, 12.3%N, 22.2%O.

2-Bromo-3-nitrofluorene. 2-Amino-3-nitrofluorene (3 gms.) was dissolved in boiling glacial acetic acid (30 mls.) which was rapidly cooled to give a mush of small crystals. To a mixture of sodium nitrite (1.4 gms.) in conc. sulphuric acid (10 mls.) was added glacial acetic acid (15 mls.). This was cooled to 10°C and the mush was added with vigorous stirring over a period of 15 minutes. The temperature was allowed to rise to 15°C and then a solution of cuprous bromide (3.5 gms.) in conc. hydrobromic acid (50 mls.) was rapidly added. Decomposition with nitrogen evolution occurred and as this abated, the solution was warmed till, after 90 minutes, 100°C was reached. The dark suspension was then poured into cold water (250 mls.) and the greenish yellow solid was filtered and dried by azeotropic distillation with benzene, before being chromatographed in benzene solution on alumina (100 gms.; diameter 1in.). A red band appeared and the eluate was collected until it became slightly tinged with red. The pale yellow eluate was then distilled to remove the benzene and the resulting solid was crystallised from petrol ether (b.p. 100-120°C) or glacial acetic acid as pale yellow lathes (1.25 gms., m.p. 119°C). The mother liquors yielded a further quantity (0·25 gms.) of comparable purity, i.e. a yield of 41%.

3-aminofluorene. A mixture of 2-bromo-3-~~amino~~nitrofluorene (1.2 gms.) and stannous chloride (4.5 gms., $SnCl_2$, $2H_2O$) in glacial acetic acid (10 mls.) and conc. hydrochloric acid (10 mls.) was boiled under reflux for 150 minutes, further additions of hydrochloric acid (5 mls.) being made every half hour. The solution was poured into an equal volume of cold conc. hydrochloric acid whereupon the stannichloride crystallised. This was filtered off and suspended in 20% caustic soda solution. The white solid which appeared was extracted with ether (2x50 mls.) which developed a blue fluorescence. After drying over sodium sulphate and removing the ether, the pale yellow solid was dissolved in petrol-ether, b.p. 80-100°C. The amine (0.35 gms.) crystallised as yellow needles (m.p. 149-50°C, Lit 151-2°C). A further crop (0.14 gms.) raised the yield to 0.49 gms. or c. 60% of theoretical.

$C_{13}H_{11}N$ requires 7.7%N.

Found 7.2%N.

The N-acetyl derivative melted at 183-4°C (Lit 186°C).

$C_{15}H_{13}NO$ requires 6.3%N.

Found 6.0%N.

The amine is, therefore, substantially pure.

3-Bromofluorene. 3-Amino-fluorene (0.3gms.) was dissolved in conc. hydrobromic acid (2 mls.) containing water (3 mls.), with warming. The suspension obtained on cooling was diazotised with saturated sodium nitrite solution in the usual way at 0°C. This diazo-solution was then added to cuprous bromide (0.3 gms.) dissolved in conc. hydrobromic acid (10 mls.). After slowly raising the temperature of the reaction mixture to 100°C it was poured into water (50 mls.). The products were extracted into benzene and this was washed with (1) 2N- caustic soda solution (2) 2N-hydrochloric acid and (3) water. After drying by azeotropic distillation with benzene the product was chromatographed in benzene on alumina. A pale yellow band was the only band eluted and the product from this band, when crystallised from aqueous methanol, had a melting point of 70-2°C. It was obviously impure and the bromine analysis was low.

$C_{13}H_9Br$ requires 32.6% Br

Found 28.7% Br.

Drying below the melting point at room pressure was not very successful as the material seemed to retain solvent avidly. It was also somewhat volatile and an attempt at drying under reduced pressure was therefore damaging to the small yield.

The mercuration of fluorene. (1) (Cf. Miller and Bachman, loc.cit). Fluorene (80 gms.) was ground with mercuric acetate (160 gms.) and the mixture was fused at 140-5°C and the glacial acetic acid produced was condensed and weighed. Miller and Bachman claim completion after 25 mins. In fact after 45 mins. only 60% of the required amount of acetic acid was evolved. The mercurichloride was formed by Miller and Bachman's method and was washed with large quantities of hot alcohol, acetone, acetic acid and warm benzene. The pink powder left after prolonged drying at 70°C weighed 145 gms. The bromination of part of this mercurichloride (80 gms.) was then carried out using the Miller and Bachman procedure. The precipitation of the mercuric salts by hydrogen sulphide unexpectedly gave a buff coloured precipitate, which was not sulphur, instead of the expected black mercuric sulphide. After hot filtration and several extractions of the residue with hot glacial acetic acid, the combined filtrates were concentrated and on cooling yielded crystals, m.p. 150-5°C. Purification of these was attained by recrystallisation from the following solvents in rotation (1) petrol-ether, b.p. 80-100°C, (2) benzene/methyl alcohol (1:1), (3) glacial acetic acid. The irregular plates thus obtained, m.p. 163°C gave the analysis:

Found 49.2% Br.

$C_{13}H_9Br$ requires 32.6% Br, and

$C_{13}H_8Br_2$ requires 48.8% Br.

No trace of a lower melting substance possessing the solubilities claimed by Miller and Bachman for their compound, m.p. 92-4°C could be found.

The mother liquor from the crude solid was poured into water and the dark oil produced solidified on standing overnight. The supernatant liquid was decanted and extracted with benzene and this benzene was added to a solution of the solidified oil in benzene. After azeotropic distillation the dark benzene solution was chromatographed on alumina (200 gms./1" diameter). Separation of a pinkish band occurred on elution with benzene containing 10% petrol ether. No other bands other than those strongly adsorbed were observed. On concentrating the eluate of the pinkish band a semi-solid reddish substance was left which on crystallisation from the solvents listed above gave the solid, m.p. 163°C. The yields of pure solid, m.p. 163°C obtained bear no resemblance to those claimed by Miller and Bachman. No trace of a material m.p. 92-4°C or of any other readily purifiable substance could be obtained.

Oxidation of substance m.p. 163°C.

The solid (0.5 gms.) was dissolved in the minimum amount of boiling acetic acid. A solution of A.R. chromic oxide (0.5 gms.) in boiling glacial acetic acid (5 mls.) was carefully added dropwise to the first solution while it was boiled gently. A vigorous reaction occurred and the

reaction was complete in five minutes. The green solution was poured into water and the solution was extracted with ether. The yellow ether layer was dried over sodium sulphate and the yellow solid was then isolated from it by distillation of the ether. Recrystallisation from glacial acetic acid followed by petrol ether gave elongated prisms of a dibromofluorenone (0.47gms., m.p. 139.5°C).

$C_{13}H_7O$ Br requires 30.9% Br.

$C_{13}H_6O$ Br_2 requires 47.3% Br.

Found 47.3% Br.

Its 2:4-dinitrophenylhydrazone was formed in the usual way and formed orange needles (chlorobenzene), m.p. 340°C (micro).

$C_{19}H_{10}N_4O_4Br_2$ requires 10.4% N.

Found 10.4% N.

Nitration of compound, m.p. 163°C. After nitration with fuming nitric acid in glacial acetic acid at the boiling point yellow needles of a mononitrodibromofluorenone were obtained, m.p. 175-8°C. Two recrystallisation of this from glacial acetic acid gave a compound m.p. 192-3°C. A lower melting isomer seems to be present but in minor quantities

$C_{13}H_7N$ Br_2O_2 requires 3.8%N and 43.2% Br.

Found 4.1%N and 44.4% Br.

Mercuration of Fluorene (2). The alternative method (Miller and Bachman, loc.cit.) for forming fluorene mercurichloride was used. A sample was subjected to steam distillation. No fluorene distilled in 30 minutes. Bromination according to their method was then carried out. The dark solution, containing suspended solid, which was obtained at the completion of the bromine addition, was hot filtered. The residue is apparently highly insoluble organo-mercuri compounds. The acetic acid filtrate was concentrated in stages and the first crystalline fractions were separated and after washing with warm benzene were combined. The compound was recrystallised from chlorobenzene and finally nitrobenzene. Analysis showed that it contained 39.8% Br.

$C_{13}H_7Br_3Hg$ requires 39.7% Br.

The presence of mercury was shown by suspending in hot acetone and bubbling in hydrogen sulphide when a yellow precipitate of a mercuri-sulphide was obtained.

The acetic acid filtrate was finally distilled to remove all the acetic acid and the residue was added to that resulting from the benzene washings from above. Steam-distillation gave fluorene in reasonable quantity, m.p. 113°C undepressed by authentic material. No bromine containing steam volatile compound could be isolated. The residue from the steam distillation was now subjected to

distillation at 0.1mm. Hg and up to a bath temperature of 250°C. The only product to distil was a mixture of dibromofluorenes principally that m.p. 163°C previously described and a little 2:7-dibromofluorene. This was shown by oxidation of the mixture of bromofluorenes and crystallisation and chromatography of the fluorenones resulting

2-nitroterephthalic acid. Terephthalic acid (20 gms.) was suspended in conc. sulphuric acid (100 mls.) and powdered potassium nitrate (30 gms.) was added in 5 portions with stirring. The mixture after warming for 90 minutes, with occasional agitation, on the steam-bath was heated for 20 minutes at 140°C in an oil bath (170°C). On cooling and pouring into water (200 mls.) and ice (200 gms.), 2-nitroterephthalic acid was obtained. After standing a few hours filtration yielded 21 gms. of the acid m.p. 268°C. Recrystallisation is unnecessary. Yield 84%.

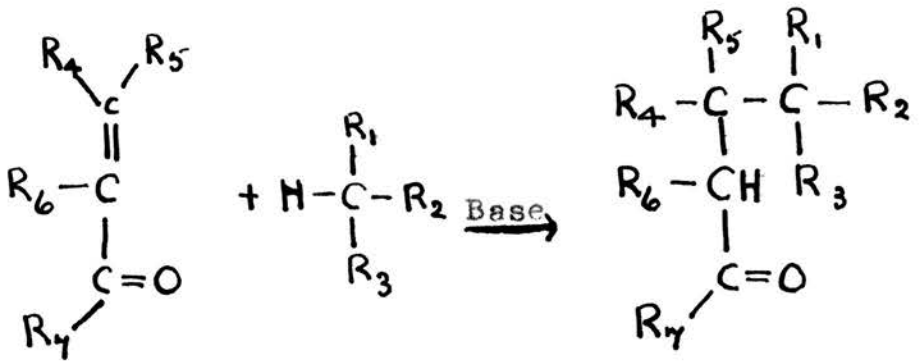
PART II

Section III

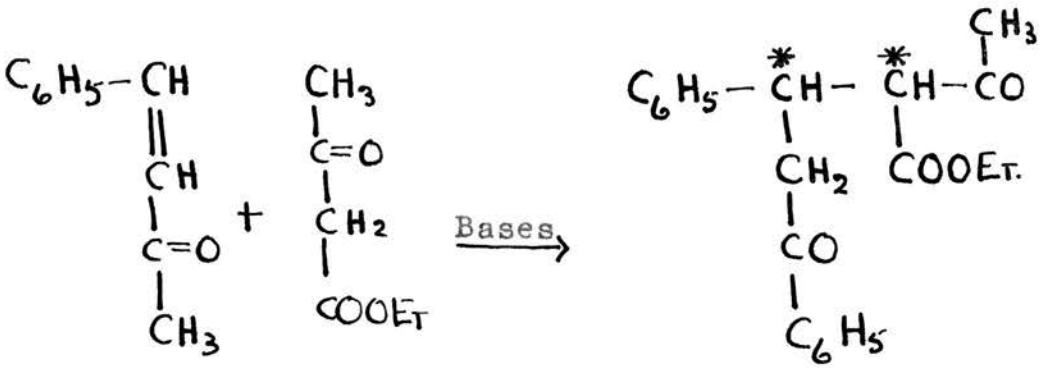
"The Michael Condensation in the Synthesis of Fluorene Derivatives"

Summary: The work described is of an exploratory nature and is calculated to indicate the synthetic possibilities of the Michael condensation in the fluorene series. The conclusions reached are fully discussed.

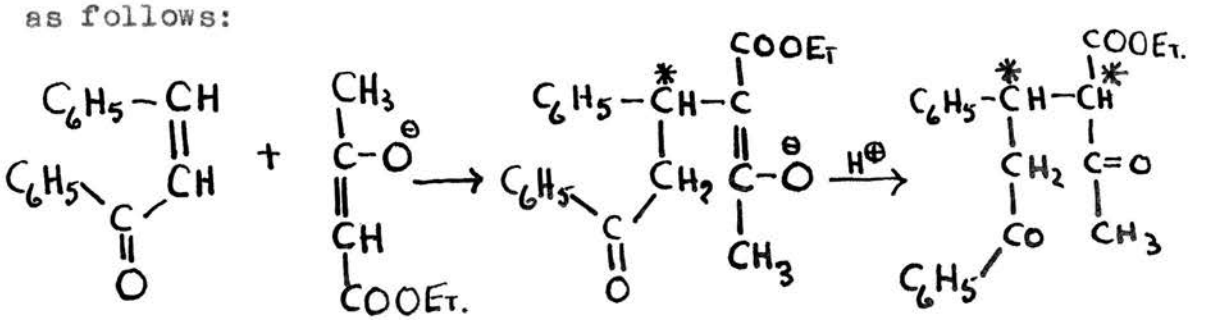
The Michael condensation is a base-catalysed reaction between one compound containing a reactive methine or methylene group and another containing an α:β-unsaturated keto, or ester or similar grouping. A carbon/carbon linkage is established between the carbon atom of the methine group and the β-carbon atom with transference of the methine hydrogen atom to the α-carbon atom.



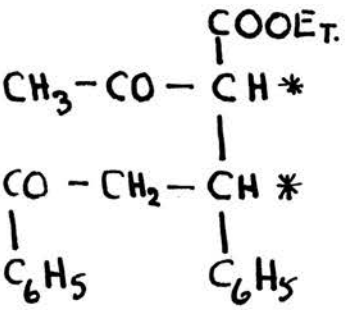
This may be exemplified by the reaction of benzylidene-acetophenone and acetoacetic ester in the presence of bases.



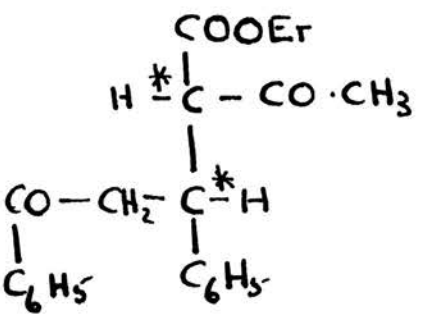
Knoevenagel (Ber., 1902, 35, 398) used diethylamine as base and obtained a product m.p. 121°C. Subsequently Kohler (Am. Chem. Journal, 1906, 37, 385) used not only diethylamine but also relatively small quantities of sodium ethoxide. In the former case his product had a melting point of 121°C and in the latter 168°C. Repetition of Knoevenagel and Kohler's work yielded only one product m.p. 168°C. The reason for this variation is most probably as follows:



There may be several discrete stages in the passage to the enolate of the Michael product, I, but for this argument I is regarded as the first significant intermediate. In I there has been developed an asymmetric carbon atom and so in the second stage, where the uptake of a hydrogen ion creates a second asymmetric carbon atom, there should be produced two compounds whose relationships may be represented by II(a) and II(b).



II(a) Racemate

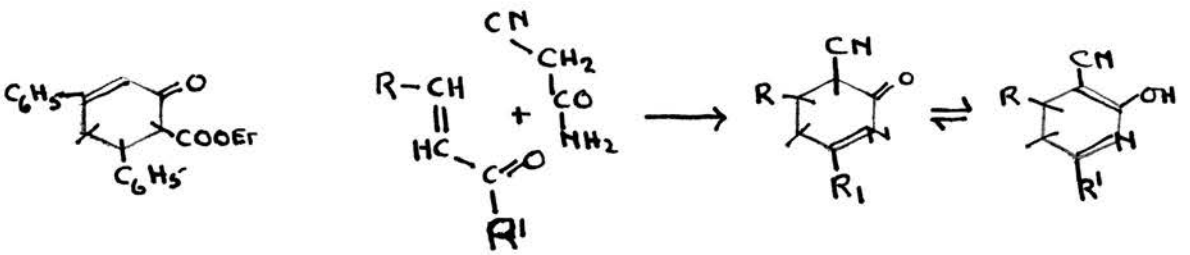


II(b) Racemate

II(a) and II(b) need not necessarily be produced in equal quantities and both are racemates. The reactivity of the hydrogen atom attached to one of the asymmetric centres makes it probable that in the presence of bases an equilibrium state between II(a) and II(b) in solution would be rapidly established. If, however, there was some cause

which induced the selective crystallisation of either component then a tendency to disturb the equilibrium would be created and the rapid equilibration would permit, eventually, the total crystallisation of one form. The important factor as to which of compounds m.p. 121°C or m.p. 168°C is obtained would appear to be which crystallised first. This is not an unprecedented phenomenon. Woodward in his recent Centenary Lecture cited the seeding of an enolate solution with either of the two components that could be obtained by the addition of a proton to the enolate ion, to give a 100% yield of the form present in the seeding crystal.

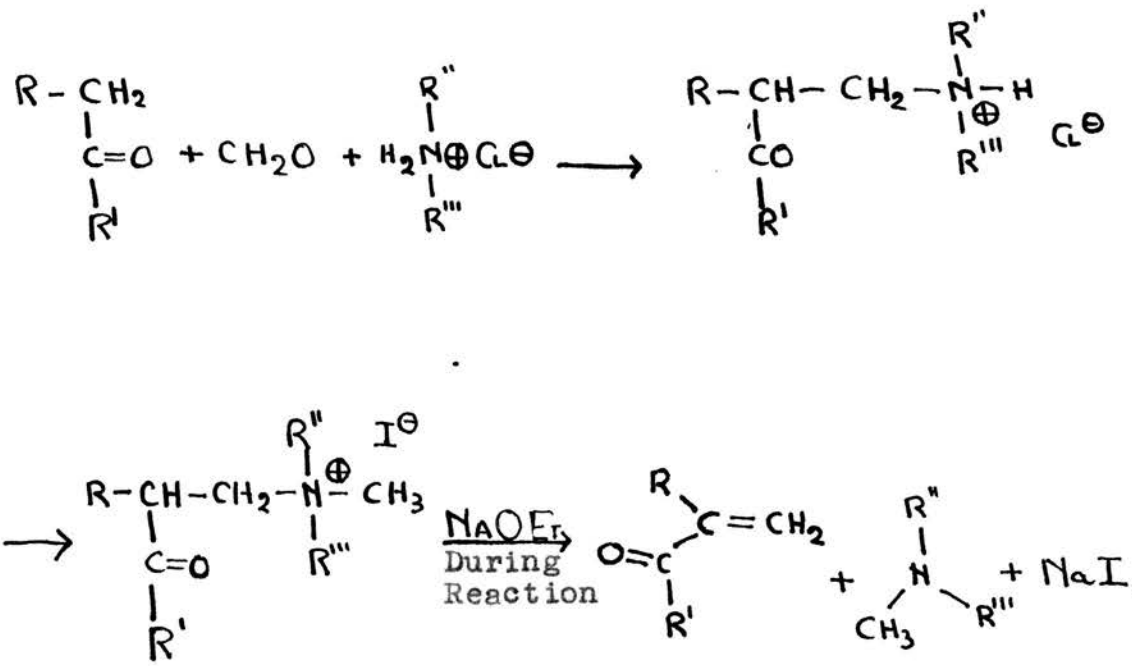
Many examples of the Michael condensation exist, e.g. the condensation of maleic anhydride with fluorene in the presence of basic catalysts (page 26). The most important reactions, however are those in which, subsequent to the Michael reaction, an internal Claisen type condensation occurs. Knoevenagel and Schmidt (Ann., 1844, 281, 58) for example treated benzylideneacetophenone with sodio-acetoacetic ester and obtained directly 3:5-diphenyl-2-carbethoxy- Δ 5:6-cyclohexene III, and it was found that the intermediates, previously mentioned, could be cyclised to the same product (Knoevenagel, loc.cit.).



III IV

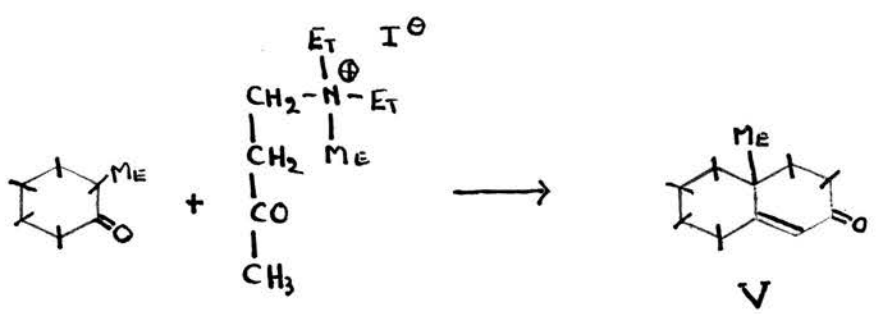
The cyclisation need not be of the Claisen type for heterocyclic molecules have been obtained. Barat (J. Ind. Chem. Soc., 1930, 7, 321) claimed that the reaction of vinyl ketones with α-cyanoacetamide yielded, by treatment with sodium ethoxide, the dihydro-2-hydroxy-3-cyanopyridine derivatives of type IV.

The principal variant introduced in recent years has been the generation of the vinyl ketone from a stable precursor during the course of the reaction. The most useful of such precursors have certainly been the Mannich-Robinson bases. These are, in general, obtained by condensing a suitable ketone containing an α-methylenic group with formaldehyde and a secondary base hydrochloride followed by treatment of the derived Mannich base with methyl iodide.

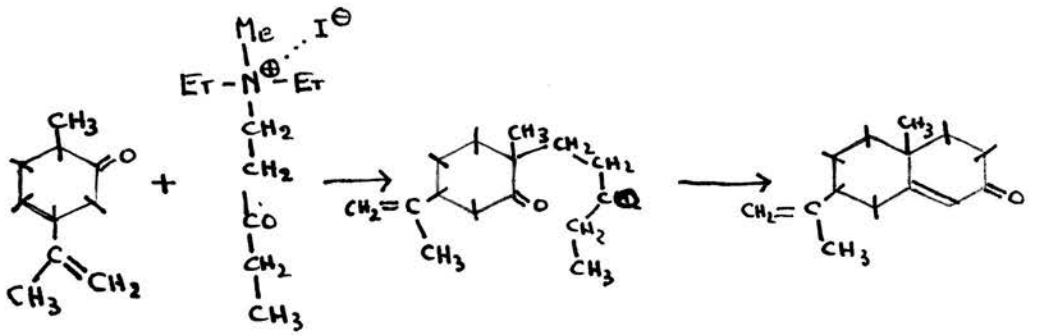


This procedure has been highly successful in the synthesis of terpenoid and steroid type compounds.

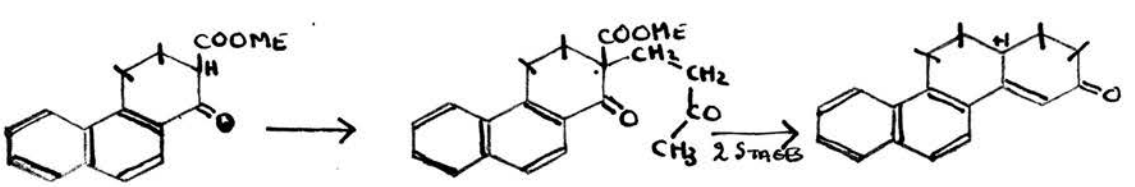
(1) Du Feu, M^{c}Quillin and Robinson (J., 1937, 53) condensed 2-methylcyclohexanone with the acetone Mannich-Robinson base to obtain the octahydronaphthalene derivative, V.



(2) Adamson, M^{c}Quillin, Robinson and Simonsen (J., 1937, 1576) condensed dihydrocarvone with the Mannich-Robinson base from methylethylketone and obtained α- and β-cyperone.

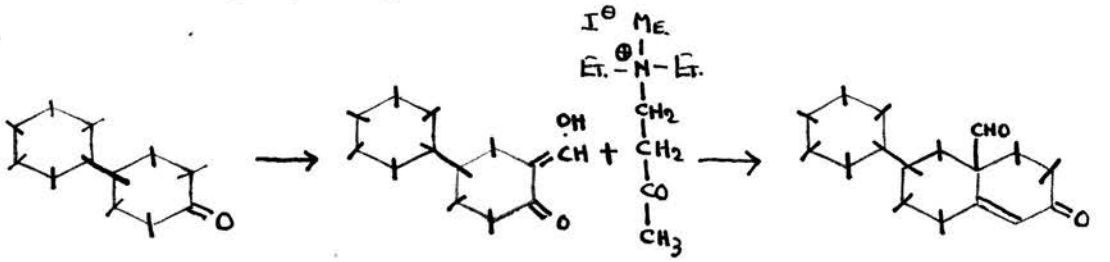


(3) Wild and Shunks (J.A.C.S., 1943, 65, 469) condensed 1-keto-2-carbomethoxytetrahydrophenanthrene VI with an acetone Mannich-Robinson base (1-diethylamino-butan-3-one methiodide) and obtained the hexahydrochrysene ketone VII.

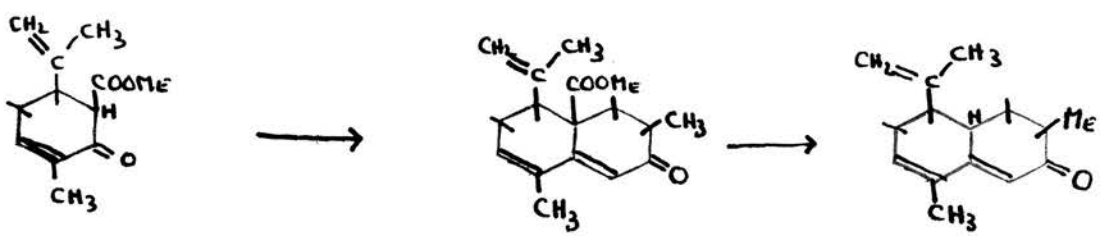


VI VII

(4) Wild and Shunks later (J.A.C.S., 1949, 71, 3446) introduced in place of the carbomethoxy group, such as in VI above, the hydroxymethylene group to activate the methine hydrogen atom as it was not only readily introduced but also readily hydrolysed.

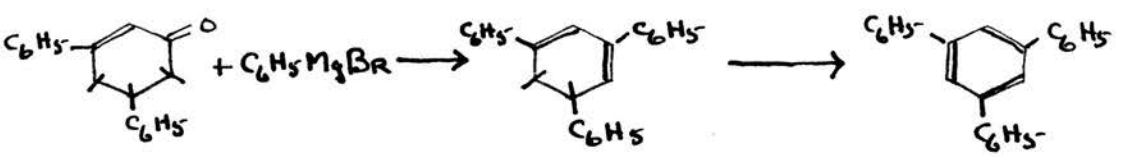


(5) J. Stafford (Cambridge University Thesis) showed that 3-carbethoxycarvone could be employed with the Mannich-Robinson base from methylethylketone to give VIII and finally IX.



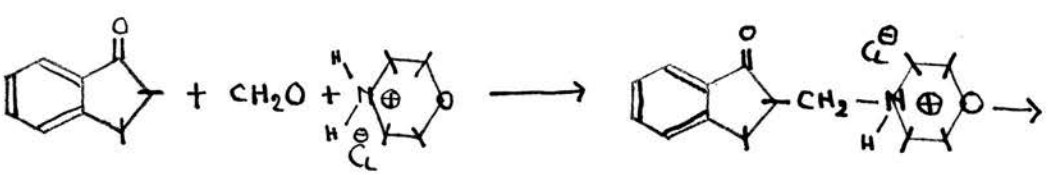
VIII IX

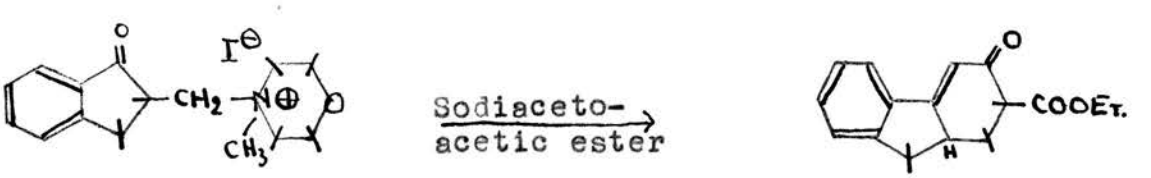
On the whole however little has been done to use these reactions for the synthesis of purely aromatic compounds. Kohler (loc.cit.) was one of the first to obtain an aromatic compound by a sequence involving Michael type condensations. He hydrolysed 2-carbethoxy-diphenylcyclohexenone, III, to 3:5-diphenylcyclohexenone, X, which after reaction with phenylmagnesium bromide and dehydrogenation of the product gave 1:3:5-triphenyl-benzene, XI.



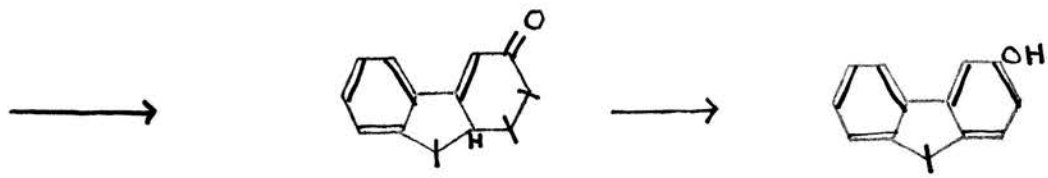
X XI

Harradence and Lions obtained 3-fluorenol XIV from hydrindone by the reaction sequence shown (J. Proc. Roy. Soc. New South Wales, 1938, 72, 284).





XII

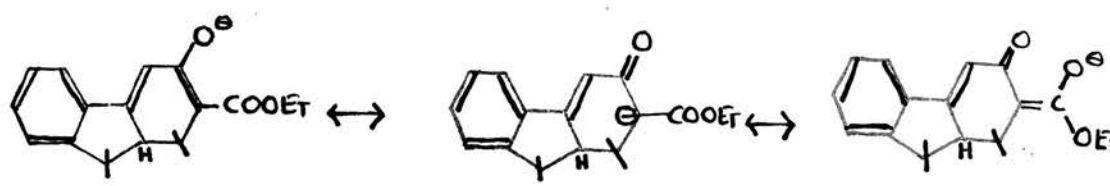


XIII XIV

In their work they preferred morpholine for the secondary base and they condensed the 2-(N-morpholinomethyl)-1-hydrindone with acetoacetic ester to obtain 2-carbethoxy-2-keto-1:2:3:1a-tetrahydrofluorene, XII, and hence 3-keto-1:2:3:1a-tetrahydrofluorene, XIII. The Michael condensation is a fruitful source of α:β-unsaturated ketones of the cyclohexenone type and is therefore particularly adapted to the synthesis of phenols by dehydrogenation (Horning, Horning and Walker, J.A.C.S., 1947, 69, 1359; ibid. 1949, 71, 169) but little attempt has been made to use it for the Synthesis of hydrocarbons. It is apparent that reduction of the cyclohexenones to cyclohexanols followed by dehydration and dehydrogenation should give aromatic hydrocarbons. Studies along these lines have been initiated.

The first step was the repetition of part of Harradence and Lions' work. Minor differences were observed but these might have been due to the differences in the scale of operation. The passage from XII to XIII was

achieved by acid hydrolysis in preference to the heating with glycerol at 180°. Depending on the conditions used XIII, or an acidic side product, m.p. 137°C, were obtained. An attempt was made to use XII in the typical substitution reactions of β-ketoesters. In its reaction with bromine, substitution of one hydrogen atom occurred; presumably the hydrogen atom on the α-carbon atom was replaced. This bromo-compound was treated with alkali in an attempt to obtain 3-hydroxyfluorene-2-carboxylic acid by dehydrohalogenation and hydrolysis of the ester group. No pure product was isolated. The attempted alkylation and acylation of the enolate of XII were abortive. This was presumably due to the extended conjugated system in the enolate ion in which there was insufficient charge localisation on any carbon atom to permit reaction in the manner desired.

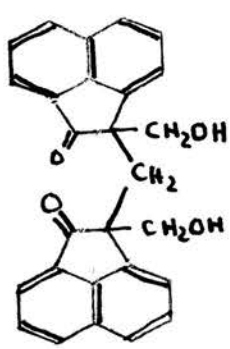


(a) (b) (c)

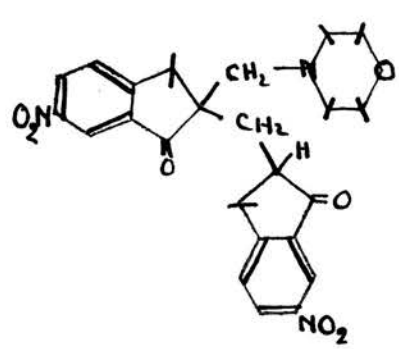
The α:β-unsaturated group serves to stabilise the canonical from (a) and the resonance hybrid will therefore have a much higher charge localisation on the oxygen atom than in

a normal saturated β-ketoester. The reaction with alkyl or acyl halides probably occurred therefore to form the O-ether or ester which on adding water or removal of the base reverted to the starting material.

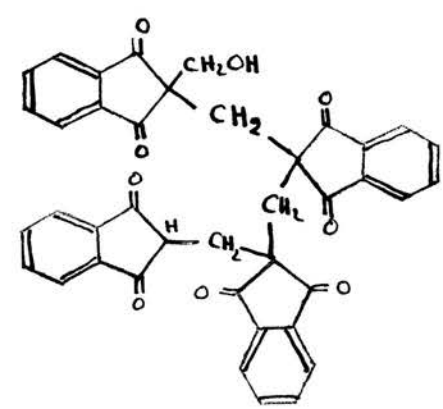
An attempt was made to extend this synthetic method to substituted hydrindones. 6-Nitro-1-hydrindone was selected and it was found to give 2-(N-morpholinomethyl)-6-nitro-1-hydrindone hydrochloride dihydrate in the normal manner but any attempt to obtain the Mannich base by alkali treatment of the hydrochloride gave coloured solutions. This sensitivity to bases was not inexpected as the original ketone was also extremely unstable to alkali, but the fact that not even sodium acetate gave the desired product was surprising. Ammonia gave in addition to a coloured solution, a small quantity of a crystalline material which proved to be analogous to that obtained by Harradence and Lions and had probably the structure XV.



XVII



XV



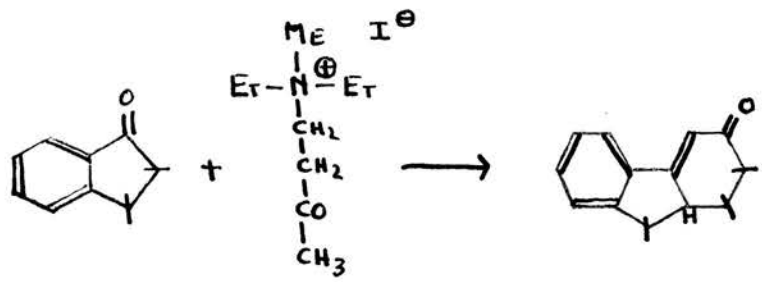
XVI

An attempt was made to form the Mannich base from 1:3-diketohydrindene but the only product isolated contained no nitrogen and had an analysis which indicated that the soul reaction was between formaldehyde and the ketone. A possible structure is XVI. This difficulty is not unprecedented as 2-hydrindone and 2-tetralone failed to give a Mannich base. Gow (Edinburgh thesis) attempted to prepare the Mannich base of acenaphthenone and it appears likely that the structure XVII is most compatible with the analysis for his compound.

$C_{17}H_{20}O_4$ requires 79.4%C and 4.9%C.

Found 78.9%C and 4.7%H.

The synthesis of 3-ketotetrahydrofluorene by the condensation of hydrindone with the Mannich-Robinson base from acetone was now attempted.



The only products isolated appeared to be derived from the self-condensation of 1-hydrindone. The use of 1:3-diketohydrindene and 1:2-diketohydrindene also gave basic condensation products of the ketones.

From these experiments it became apparent that the formation of a Mannich base is controlled by the competition of a reaction between formaldehyde and the ketone and the true Mannich reaction and that therefore best results are obtained by the use of a ketone in which the α-methylene group is of low but sufficient reactivity, e.g. acetone gave excellent results (Wild & Shunks, loc.cit.). The reaction of the Mannich-Robinson base once formed with a ketone in the Michael condensation is dependent on the rate at which it gives the vinylketone compared with the rate at which self-condensation of the other ketone occurs. The ketone should therefore give a stable enolate in the presence of bases instead of undergoing self-condensation. β-Carbethoxy or hydroxymethylene ketones seem to be the most efficacious as diketones containing a reactive methylene group seem to suffer self-condensation too readily. In hydrindone the enolate ion is not sufficiently stable and it rapidly reacts with another molecule of hydrindone rather than with the vinylketone.

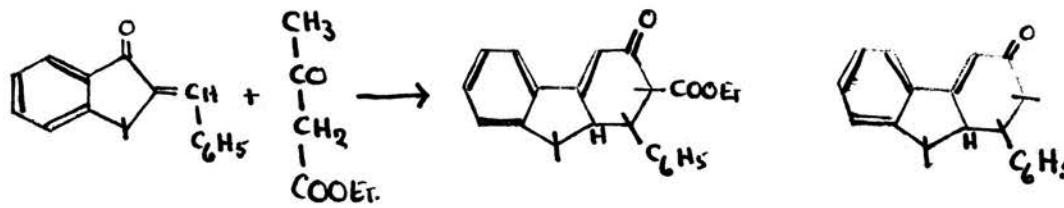
Two solutions that might be used for this problem are (1) to see how far Alexander and Underhill's (J.A.C.S., 1949, 71, 4019) conclusions regarding the kinetics of the Mannich reaction might be adapted to the synthesis of Mannich bases in difficult cases.

(2). to adapt the ketone chemically so that it becomes suitable for condensation with Mannich-Robinson bases or to form Mannich bases. Alexander and Underhill concluded that the Mannich reaction is ionic and is based on a primary condensation of formaldehyde with the amine. It might be possible to replace formaldehyde and the base hydrochloride with dialkylaminomethanol hydrochloride, thus obviating any condensation of formaldehyde and the ketone alone. The adaptions in the ketone structure that might be used are the introduction in such cases as 1-hydrindone of a carbethoxy- or hydroxymethylene group in the 2-position. In the case of the formation of the Mannich bases of acenaphthenone the same final result could well be achieved by using tetrahydroacenaphthenones which are in effect 3-alkyl-1-hydrindones (cf. Johnson and Glen. loc.cit.).

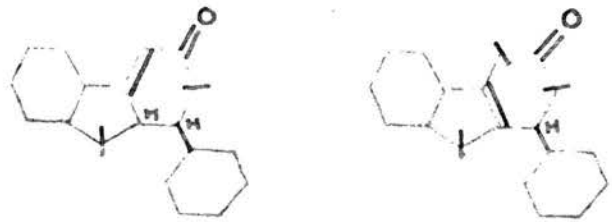
Petrow (Abs., 1929, 23, 2156; Ber., 1929, 62B, 643) passed from Δ^3:5-diphenylcyclohexenone to 3:5-diphenylcyclohexanol by reduction with sodium in alcohol. This method of synthesis was improved by substitution of hydrogenation with a Raney nickel catalyst for the metal/alcohol reduction (cf. Cornubert and Phélisse, Abs., 1949, 43, 4652). The diphenylcyclohexanol obtained (m.p. 111°C), was presumably a stereoisomer of that obtained by Petrow (m.p. 127°C); as it gave a diphenylcyclohexanone of the same

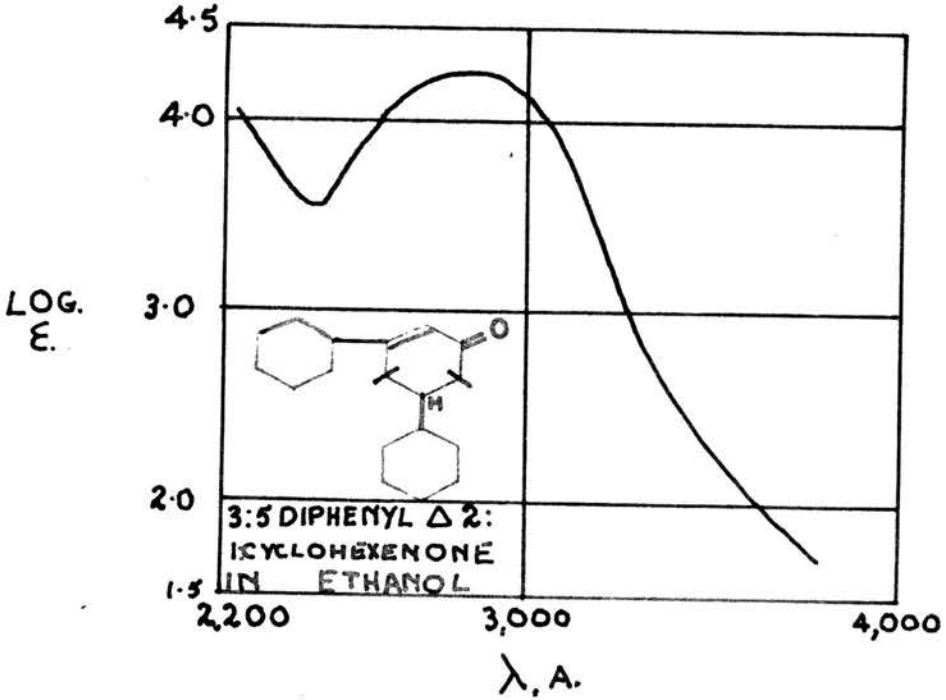
properties as that described by Petrow. The stereoisomerism must be due to the hydroxyl group and the phenyl group originally attached to the β-carbon atom of the α:β-unsaturated ketone. There was evidence of a mixture of products from the reduction which probably gave both isomers. The 3:5-diphenylcyclohexenone was obtained by an improved procedure. The diphenylcyclohexanol was dehydrated with phosphorus pentoxide in xylene and the diphenylcyclohexene, which was not isolated, was dehydrogenated to m-terphenyl with chloranil. The reaction model is complete.

Work which was intended to yield 1-phenylfluorene and 7-phenylfluoranthene was commenced but was not completed due to lack of time. The reactions may be represented schematically as below.



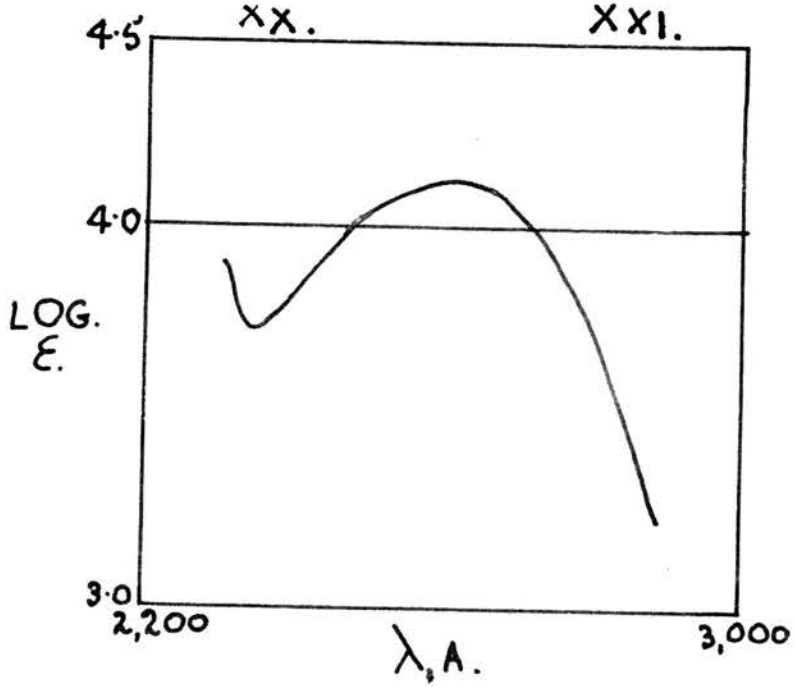
XVIII XIX XX





MAXIMUM		MINIMUM	
λ	LOGε	λ.	LOGε
2,850	4·27	2,450	3·51

XX.



XXI.

MAXIMUM		MINIMUM	
λ	LOGε	λ	LOGε
2,610	4·12	2,345	3·72

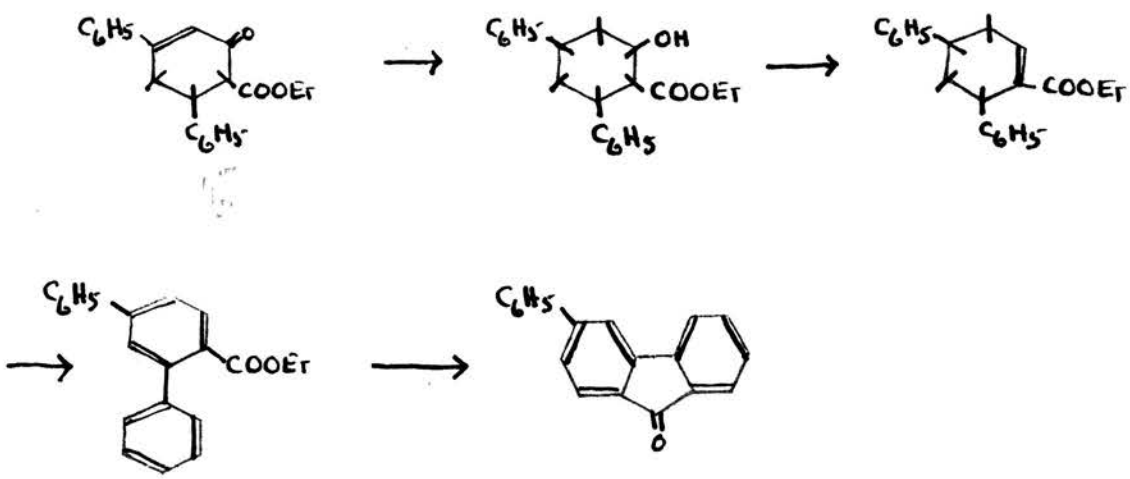
Benzylidene hydrindone, XVIII, (Kipping, loc.cit.) was reacted with sodioacetoacetic ester in alcohol and yielded 1-phenyl-2-carbethoxy-3-keto-1:2:3:1a-tetrahydrofluorene, XIX. This on treatment with acid was decarboxylated to what was thought to be the 1-phenyl-3-keto-1:2:3:1a-tetrahydrofluorene, XX. As a side product of the hydrolysis a compound m.p. 244°C was obtained which proved to be identical with the polymer of benzylidene hydrindone obtained in the presence of relatively large quantities of bases (see below). The ketone obtained from the hydrolysis was hydrogenated under the condition used for diphenylcyclohexenone but gave only a ketonic substance. In an endeavour to discover the reason for this failure, the absorption spectra of the ketone was compared with that of diphenylcyclohexenone (see opposite). It was found that the diphenylcyclohexenone had a typical α:β-unsaturated ketone spectra while the ketone, supposedly of structure XX, had not. If, therefore, immediately became apparent that the five-membered ring seems to have caused a migration of the double bond, perhaps to 1a, 4a, XXI, and the failure to obtain reduction of the ketonic group was consequently explicable, for Raney nickel is specific for α:β-unsaturated ketones but seldom for simple ketones. Time and material did not permit the Clemmensen reduction and dehydrogenation of XXI to 1-phenylfluorene.

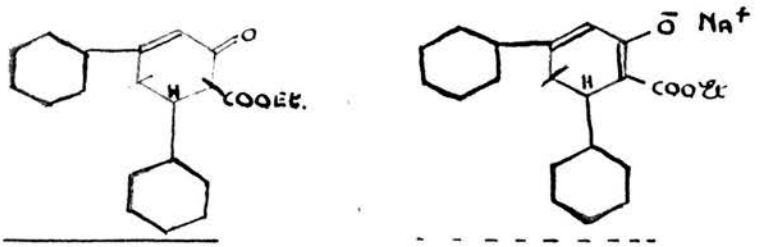
Two side products have been obtained from the acid hydrolysis of the β-carbethoxycyclohexenones. In the case of 2-carbethoxy-3-ketotetrahydrofluorene an acidic substance m.p. 137°C was obtained. Its analysis was compatible with the molecular formula $(C_{10}H_8O)_x$ but the molecular weight (Micro Rast) was intermediate between the monomer and the dimer, although much closer to the monomer. $C_{10}H_8O$ is the molecular formula of 2-methylene-1-hydrindone an intermediate in the Michael condensation leading to 2-carbethoxy-3-ketotetrahydrofluorene. Similarly the product m.p. 244°C, obtained from 1-phenyl-2-carbethoxy-3-ketotetrahydrofluorene analysed for and was identical with a polymer (probably a dimer) of one of the reactants in the primary Michael condensation. It seems likely that in addition to decarboxylation acid treatment causes the reversal of the Michael condensation. The abnormal molecular weights found for the two products may be due to further polymerisation in the hot camphor.

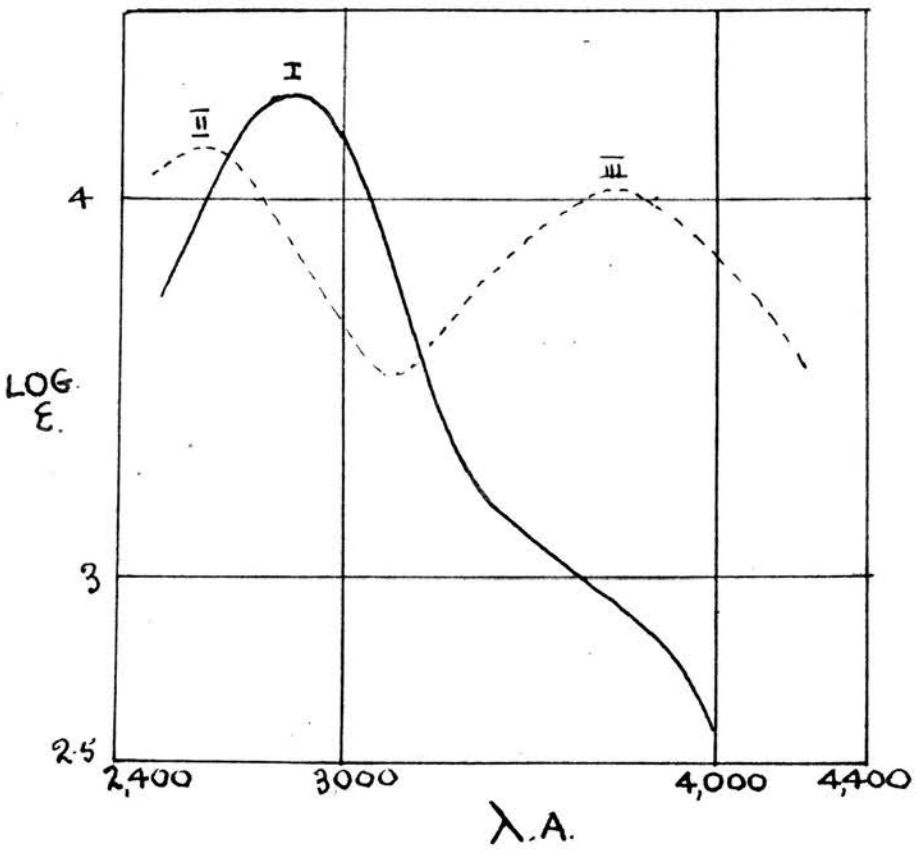
The hydrolysis and decarboxylation of the carbethoxy-cyclohexenones might be better achieved by alkaline treatment. Recently Downes, Gill and Lions (J.A.C.S., 1950, 72, 3464) and Gill and Lions (ibid., 3468) have described such hydrolyses which they applied immediately following the Michael condensation without isolating the carbethoxycyclohexenone. This latter arrangement although

undesirable in many ways avoids the difficulty that in some cases a mixture of carbethoxycyclohexenones is obtained due to the configuration of the carbethoxy group (i.e. cis or trans to another group in the ring). Although usually only one such isomer is isolated, there often remains after the purification a residual oil which on hydrolysis gives yields of the cyclohexenone comparable with those from the pure product. (This observation was made several times in this work but the details are not given in the experimental section).

An attempt was made to synthesise 3-phenylfluorenone by the intended formation of 2:4-diphenylbenzoic acid from 3:5-diphenyl-2-carbethoxycyclohexenone by the reaction sequence shown below.







Maximum.	λ_{max}	Log. ε.
I	2,870	4·25
II	2,520	4·14
III	3,720	4·02

The initial reduction stage was attempted by three methods

(1) The Clemmensen reduction.

(2) Lithium aluminium hydride.

(3) Hydrogenation.

The Clemmensen reduction was totally unsuccessful and the principal reaction appeared to be simple acid hydrolysis to diphenylcyclohexenone. The action of lithium aluminium hydride and hydrogenation both augmented the hydrogen value in the analysis of products but there was no evidence that the 2-carbethoxy-3:5-diphenylcyclohexanol was produced in a satisfactory manner. Further work along these lines would however be worthwhile in the future.

The absorption spectra of III and its sodium enolate XXI in alcohol were determined (see opposite). Two prominent maxima were present in the enolate spectrum and one of these extended well into the visible region. The absorption spectra is compatible with the extended conjugated system as indicated.

These preliminary studies with their indications of bond migrations and Michael condensation reversals are valuable for they show the pitfalls that must be avoided in any future work. The successful passage from the cyclohexenone to the benzene derivatives opens a large field of synthetic work in the aromatic series in view

of the many methods available for the synthesis of cyclohexenones (cf. Prelog and Zimmerman H.C.A., 1949, 32, 2360; Woods and Reed, J.A.C.S., 1949, 71, 1348; Woods and Tucker, ibid., 70, 2174, 3340).

Experimental Section

2-Morpholinomethyl-1-hydrindone hydrochloride (cf. Harradence & Lions, loc.cit.).

A mixture of hydrindone (6 gms.), morpholine hydrochloride (6.6 gms.), paraformaldehyde (1.5 gms.) in alcohol (9 mls.) was boiled under reflux for 2 hours. After cooling the hydrochloride of the Mannich base was precipitated by adding dry ether (20 mls.). Filtration gave the white hydrochloride (11.3 gms. Cf. H. and L. 10 gms.) which contained very little morpholine hydrochloride and was sufficiently pure for the next stage. Recrystallisation from alcohol containing ether gave plates m.p. 162°C (lit. m.p. 162°C).

2-Morpholinomethyl-1-hydrindone methiodide. 2-Morpholinomethyl-1-hydrindone hydrochloride (11 gms.) was suspended in caustic soda solution (40 mls./4 N) and sufficient potassium chloride was added to saturate the solution. Extraction with ether, followed by drying of the ethereal layer with sodium sulphate gave a yellow oil (8.5 gms.) after removal of the ether. This oil was dissolved in methyl iodide (130 gms.) and the solution was cautiously warmed on the water bath for a few minutes. After standing at room temperature for 90 minutes the solid mass was placed in a basin in a vacuum desiccation and the methyl iodide was removed leaving the methiodide (13 gms.).

2-Carbethoxy-3-keto-1:2:3:1a-tetrahydrofluorene

The methiodide (5.15 gms.) was added to a solution of ethyl acetoacetate (2.87 gms.) in absolute ethanol (15 mls.) in which sodium (0.4 gms.) had been dissolved. After boiling for three hours the solution was cooled and filtered and the product was recrystallised from alcohol (yiled 1.45 gms.). A further quantity (0.4 gms.) was obtained from the original mother liquors by pouring into dilute acid and then chromatographing the resulting oil in benzene solution on alumina. Total yield of a product m.p. 159°C was 1.85 gms. (Lit. 1.5 gms.).

The Hydrolysis of 2-carbethoxy-3-ketotetrahydrofluorene by acid

(a) 3-Keto-1:2:3:1a-tetrahydrofluorene was obtained by hydrolysis of 2-carbethoxy-3-ketotetrahydrofluorene (1.26 gms.) in dioxan (10 mls.) solution containing hydrochloric acid (5 mls. conc. acid in 2 mls. water). Additions of acid (2 mls. conc. hydrochloric acid in 2 mls. dioxan) were made every half hour during the period of boiling (3 hours). On dilution with water (50 mls.) an oil was precipitated and this was extracted into ethereal solution (2x50 mls.) which, after drying over sodium sulphate, left a yellow oil on removal of the ether. The oil was triturated with cold methanol (10 mls.) and a crystalline residue (0.1 gms.) was left undissolved.

This proved to be unchanged starting material m.p. 156-7°C. The methanol solution gave a 2:4-dinitrophenylhydrazone, m.p. 250°C, which crystallised as blood red needles from xylene. On removal of the methanol under reduced pressure 0.65 gms. of a yellow oil was obtained. This when triturated with petrol-ether solidified and recrystallisation from petrol-ether/ethyl acetate or petrol-ether/ether mixtures gave, after seeding, rosettes of prisms m.p. 97-8°C. (H. & L. give m.p. 100°C after distillation).

(b) An acidic substance was obtained by hydrolysis of 2-carbethoxy-3-ketotetrahydrofluorene (1 gm.) in a mixture of sulphuric acid (1 ml.), acetic acid (2 mls.) and water (2 mls.). The solution finally obtained after boiling for 90 minutes was poured into water (15 mls.) and the products were obtained by extraction with ether (25 mls.). The ether layer was shaken with cold 2N caustic soda solution (5 mls.) and this was acidified and thoroughly chilled. The solid (0.15 gms.) obtained was recrystallised from aqueous methanol and had a melting point of 137°C.

$C_{10}H_8O$ requires 83.3%C; 5.6%H and M.Wt 144.

Found 83.1%C; 5.8%H and M.Wt. 176.

The solution in 2N caustic soda was colourless.

The attempted acylation and alkylation of 2-carbethoxy-3-ketotetrahydrofluorene.

The 2-carbethoxy-3-ketotetrahydrofluorene (1 gm.) was dissolved in hot ethanol (15 mls.) containing an excess of sodamide forming thereby the yellow sodium enolate. The acyl or alkyl halide in considerable excess (2-10 moles.) was added and reaction was allowed to proceed at the boiling point for periods as long as four hours. Usually the yellow colour faded due to the formation of sodium halide but always on cooling and adding water the compound crystallising proved to be the unchanged fluorene derivative. The halides used were methyl iodide, benzoylchloride, phenacylchloride, O-nitrobenzylchloride and p-nitrobenzylbromide and apart from their degradation, e.g. p-nitrobenzylbromide to the alcohol, no other reaction occurred.

The product from methyl iodide, m.p. 159°C, gave the analysis shown.

$C_{17}H_{18}O_3$ requires 71.3%C and 6.4%H.

Found 74.2%C and 6.1%H.

whereas

$C_{16}H_{16}O_3$ requires 74.8%C and 6.3%H.

2-Bromo-2-carboxy-3-ketotetrahydrofluorene

2-Carbethoxy-3-ketotetrahydrofluorene (0.1 gms.) was dissolved in alcohol (4 mls.) and a solution of bromine

(0.5 mls.) in alcohol (10 mls.) was added dropwise to the hot solution until no more bromine was absorbed. On cooling and adding water the bromoderivative was precipitated. Recrystallisation from ethanol and then petroleum ether gave small white prisms m.p. 158°C.

$C_{16}H_{15}O_3Br$ requires 23.8% Br)
Found 24.2% Br).

2-Morpholinomethyl-6-nitro-1-hydrindone hydrochloride

6-Nitro-1-hydrindone (2.88 gms.) was dissolved in ethanol (5 mls.) and a mixture of morpholine hydrochloride (2.13 gms.) and paraformaldehyde (0.62 gms.) was added. After boiling under reflux for 30 minutes the solution was cooled and dry ether (20 mls.) was added causing two layers to develop. Warming under reflux for a further 30 minutes caused the lower layer to crystallise and the solid was removed by filtration. Recrystallisation from ethanol/ether was very unsatisfactory but recrystallisation from 95% ethanol gave extremely fine crystals m.p. 126°C with resolidifaction at 130-5°C and further melting at 170°C. This phenomenon was due to hydration.

$C_{14}H_{17}O_4N_2Cl$ requires 11.3% Cl and 9.0%N.
$C_{14}H_{17}O_4N_2Cl_12H_2O$ requires 10.2% Cl and 8.0%N.
Found 10.3% Cl and 8.0%N.

2-Morpholinomethyl-6-nitro-1-hydrindone

The only pure product isolated by the action of ammonia on the hydrochloride was that corresponding to the side product of the action of alkali on 2-morpholinomethyl-1-hydrindone. It had a melting point of 208°C.

$C_{24}H_{23}O_7N_3$ requires 61.9%C and 5.0%H.

Found 61.6%C and 5.0%H.

The Mannich Reaction of 1:3-diketohydrindene

1:3-diketohydrindene (1.5 gms.), morpholine hydrochloride (1.3 gms.) and paraformaldehyde (0.35 gms.) were suspended in ethanol (5 mls.). On gentle warming on the water bath a product immediately separated which proved to be extremely insoluble even in nitrobenzene. Purification by digestion with boiling acetic acid gave a pale yellow but not apparently crystalline product. On heating it became crimson but did not melt till the temperature exceeded 300°C. On suspending in alkali a red solution was obtained and there was no nitrogen or chlorine present.

$C_{81}H_{51}O_{18}$ requires 74.0%C and 4.0%H.

$C_{40}H_{26}O_9$ requires 73.9%C and 4.0%H.

Found 73.6%C and 4.1%H.

1-Diethylamino-butan-3-one-methiodide. This was prepared from 1-diethylaminobutan-3-one (Wild and Shunks, loc.cit.) by the method of Du Feu, M^{c}Quillin and Robinson (loc.cit.).

The Reaction of Hydrindone and 1-diethylamino-butan-3-one-methiodide

Hydrindone (1.32 gms.) was dissolved in ethanol (15 mls.) and the Mannich-Robinson base (3.0 gms.) was added followed by finely powdered sodamide. The mixture was warmed gently and was finally boiled for 45 mins. under reflux. The solution was then poured into 5% aqueous ammonium chloride solution (50 mls.). The deposited solid was taken up in benzene and subjected to chromatography on alumina. A yellow band which was eluted first gave a high melting solid ($> 345^{\circ}C$) which gave the colour reactions of truxene (e.g. a dark green colour with sulphuric acid containing a little nitric acid. Truxene has a melting point of 366-8°C. A second band gave a little of a dark brown solid which, although ketonic in reaction to 2:4-dinitrophenylhydrazine, did not contain 3-ketotetrahydrofluorene but was probably impure anhydrobis-hydrindone. Self-condensation of hydrindone seemed to be the most significant reaction and all modifications of this procedure confirmed it.

The substitution of 1:3-diketohydrindene or 1:2-diketo-hydrindene for hydrindone with considerable amelioration of conditions gave reaction products whose properties were identical with the products of the action of bases on the starting ketones.

1-Benzoyl-1-phenyl-3-carbethoxy-n-propylmethylketone

This was made by the method of Knoevenagel (loc.cit.) and Kohler (loc.cit.) using diethylamine to catalyse the reaction of benzylideneacetophenone and acetoacetic ester. The product obtained had a melting point of 168°C and appeared to be an isomer of the product, m.p. 124°C, obtained by Kohler and Knoevenagel. Kohler obtained such an isomer using a catalytic quantity (0.1 moles.) of sodium ethoxide in place of the diethylamine.

$C_{21}H_{32}O_4$ requires 74.5%C and 6.6%H.

Found 74.1%C and 6.5%H.

3:5-diphenyl-2-carbethoxy- Δ 5:6-cyclohexenone. This was prepared by both the methods of Knoevenagel, i.e. in one effective stage from benzalacetophenone and sodioaceto-acetic ester or in two stages via the 1-benzoyl-2-phenyl-3-carbethoxy-n-propylmethylketone. It had a melting of 112°C (Knoevenagel and Schmidt, m.p. 111-2°C).

3:5-diphenyl- Δ 5:6-cyclohexenone

The hydrolytic decarbethoxylation was achieved in the following manner. The carbethoxy compound (20 gms.) was boiled in an acidic mixture (30 gms. sulphuric acid, 30 gms. water and 30 gms. acetic acid) for 3 hours. The dark red solution was poured into water (300 mls.) and the yellow oil deposited was extracted with ether and after drying

and removal of the ether was distilled under reduced pressure (0.1-5 mm. Hg. Temp. 201-7°C). The yellow viscous oil was taken up in petrol (120 mls., b.p. 60-80°C) to which sufficient ether was added to give a clear solution. On standing overnight the ketone crystallised as elongated plates, m.p. 84°C. The yield was 10-11 gms. The method of Knoevenagel and Schmidt was found to be considerably less satisfactory.

3:5-Diphenylcyclohexanol. 3:5-Diphenylcyclohexenone (5 gms.) was dissolved in ethanol (50 mls.). A suspension of Raney Nickel (Organic Synthesis) in ethanol (5 mls.) was added and hydrogenation at room temperature and a hydrogen pressure of 40 lbs./sq. ins. was carried out. Rapid assimilation of hydrogen occurred and after 30 minutes the reaction was complete. The solution of product was removed by decantation and the alcohol was distilled off under reduced pressure. Recrystallisation of the colourless oil from light petroleum/ether gave 3:5-diphenylcyclohexanol, m.p. 111°C (3.5 gms.) as slender white needles (cf. Petrow).

$C_{18}H_{20}O$ requires 85.7%C and 8.0%H.

Found 85.4%C and 8.0%H.

The alcohol was characterised by oxidation with chromic oxide in acetic acid to diphenylcyclohexanone, m.p. 140°C (Petrow 139-40°C).

M-terphenyl. 3:5-Diphenylcyclohexanol (2 gms.) was dissolved in xylene (10 mls.) and phosphorus pentoxide (2 gms.) was added. The xylene was boiled under reflux for 2 hours and during this period the phosphorus pentoxide darkened. The xylene layer was decanted on to the chloranil (2 gms.) and this mixture was now boiled for a further 2 hours. The xylene was distilled to 5 mls. and then benzene 10 mls. was added. After cooling and filtering the filtrate was chromatographed on alumina (100 gms./1" diameter). A band fluorescing in ultra-violet light was rapidly eluted and this yielded m-terphenyl (1.2 gms.), m.p. 86°C after removal of the benzene and recrystallisation from methanol at 0°C.

$C_{18}H_{14}$ requires 93.9%C and 6.1%H.

Found 93.4%C and 6.3%H.

Characterisation of 3:5-diphenylcyclohexenone. This formed a 2:4-dinitrophenylhydrazone in the normal manner. On recrystallisation from acetic acid carmine needles, m.p. 223°C were obtained.

$C_{24}H_{20}O_4N_4$ requires 13.1%N.

Found 12.8%N.

It also formed a hydrazone which crystallised from alcohol as slender needles, m.p. 163°C.

$C_{18}H_{18}N_2$ requires 82.4%C and 6.9%N.

Found 81.3%C and 6.8%H.

Reduction of the carbethoxydiphenylcyclohexenone

(1) By the Clemmensen method. The variant of the Clemmensen method in which two liquid phases are present in the reaction vessel, was used. The carbethoxydiphenylcyclohexenone (10 gms.) was dissolved in hot toluene (75 mls.) and this was added to lightly amalgamated granulated zinc (30 gms.) in 50% hydrochloric acid (50 mls.). The mixture was boiled vigorously for 16 hours and every 90 minutes conc. hydrochloric acid (5 mls.) was added). The toluene layer was then separated and the solvent was removed after drying. The resulting yellow oil was triturated with ice-cold methanol and eventually some of the starting material (4 gms.) was obtained or a solid m.p. 108-110°C. The methanol soluble fraction was then isolated by removal of the methanol before being chromatographed on alumina in benzene solution. Only two products were isolated in a relatively pure state from the column. They were the starting material (c. 1 gm.) and some of its decarboxylation product 3:5-diphenylcyclohexenone, m.p. 79-80°C.

$C_{18}H_{16}O$ requires 87.1%C and 6.5%H.

Found 86.5%C and 6.1%H.

Although obviously slightly impure it yielded the expected 2:4-dinitrophenylhydrazone, m.p. 223°C.

That no evident reduction had occurred was demonstrated by repeating the process without the zinc when substantially the same results were obtained.

(2) By Lithium-aluminium-hydride. The lithium-aluminium-hydride was the commercial product and was found to be only slightly soluble in ether. Consequently the reaction was carried out as follows.

2-Carbethoxydiphenylcyclohexenone (2 gms.) was dissolved in ether (50 mls.) and the lithium-aluminium-hydride (a 1000% excess) was placed over glass wool in a extractor. The lithium-aluminium-hydride was then extracted from the commercial material into the reaction flask by the boiling ether. A yellow solid separated from the ether and after 30 mins. when the reaction appeared complete water (50 mls.) was added to the ether. The aqueous layer was acidified with dilute hydrochloric acid and the ether was separated. A solid substance of low solubility was obtained, on concentration, in poor yield.

$C_{21}H_{24}O_3$ requires 77.7%C and 7.4%H.

Found 77.5%C and 7.1%H.

It had a melting point of 220°C.

The remaining ether soluble material was taken up in benzene after complete removal of the ether, and was chromatographed on alumina. Fluorescent oils were obtained on elution of the column with benzene, and benzene/ethanol mixtures.

(3) Hydrogenation with Raney nickel catalyst. The compound in alcohol solution was hydrogenated with a Raney Nickel catalyst in alcohol suspension at room temperature and 60-70 lbs. per sq. ins. hydrogen pressure. Rapid uptake of hydrogen occurred and after one hour constant pressure was obtained. The alcohol solution was decanted and the product, after removal of the alcohol, was subjected to distillation at 272-5°C (bath temp. and 0.5 mm. Hg.). The viscous oil thus obtained proved difficult to crystallise. The analysis given was

Found 78.9%C and 7.1%H.

Benzylidenehydrindone. To a mixture of hydrindone (13.2 gms.) and benzaldehyde (10.6 gms.) in ethanol (30 mls.) was added dropwise a solution of potassium hydroxide (10%) in 95% ethanol. Warming occurred and the mixture was set aside as soon as any further addition of alkali caused the solution to darken. After 6 hours the almost pure benzylidenehydrindone (18 gms.) was removed by filtration and was recrystallised from alcohol. M.p. 111°C.

If the quantity of alkali added was excessive or if any heating was applied (cf. Kipping, J., 1844, 500) then considerable quantities of a polymer of benzylidenehydrindone, m.p. 242°C, was obtained.

Dimer requires 87.3%C; 5.5%H and M.Wt. 440.

Found 87.1%C; 5.5%H and M.Wt. 576.

This polymer formed a 2:4-dinitrophenylhydrazone giving the analysis

Found 8·6%N.

A dimer mono-2:4-dinitrophenylhydrazone requires 9.0%N. No reaction with bromine in acetic acid or chloroform was observed and it dissolved in cold concentrated sulphuric acid giving a yellow solution of less intensity than the monomeric substance. On dilution of the acid solution it was returned as a fluffy precipitate.

1-Phenyl-2-carbethoxy-3-keto-1:2:3:1a-tetrahydrofluorene

Benzylidenehydrindone (2.2 gms.) was dissolved in a solution of acetoacetic ester (1.5 gms.) in ethanol (25 mls.) containing dissolved sodium (0.3 gms.). The mixture was heated for 3 hours on the steam bath and at the end of this time the mixture was cooled and treated with 10 mls. of dilute hydrochloric acid. The precipitated solid was recrystallised from alcohol giving white or slightly yellow needles, m.p. 135°C (2.8 gms.).

$C_{22}H_{20}O_3$ requires 79.5%C and 6.1%H.

Found 79.3%C and 6.1%H.

1-Phenyl-3-keto-tetrahydrofluorene

1-Phenyl-2-carbethoxy-3-ketotetrahydrofluorene (2 gms.) was dissolved in an acidic mixture (8 gms. sulphuric acid, 8 gms. water, 10 gms. acetic acid) on boiling for 3 hours.

The dark solution was poured into water (50 mls.) and the resulting yellow oil was triturated with ether. The solid that separated was filtered and recrystallised from acetic acid. It had a melting point of 244-5°C (yield 0.2 gms.). The ether layer was dried over sodium sulphate and the solvent was removed. The resulting oil was distilled (230°C/0.1 mm. Hg.) under reduced pressure and gave 0.8 gms. of a yellow oil. This was recrystallised from light petroleum/ether and gave gleaming laminae, m.p. 115°C (0.5 gms.). The oil from the mother liquors was shown to contain considerable quantities of the ketone for both the ketone, m.p. 115°C, and the oil gave a 2:4-dinitrophenylhydrazone which crystallised from xylene as blood red prisms, m.p. 250°C.

Compound m.p. 244-5°C

$C_{16}H_{12}O$ requires 87.3%C and 5.5%H.

Found 87.3%C and 5.8%H.

A mixed melting point with the benzylidene hydrindone dimer showed no depression.

Compound m.p. 115°C

$C_{19}H_{16}O$ requires 87.7%C and 6.2%H.

Found 87.5%C and 6.3%H.

2:4-dinitrophenylhydrazone, m.p. 250°C

$C_{25}H_{20}N_4O_4$ requires 12.7%N.

Found 13.0%N.

2-Bromo-2-carbethoxy-1-phenyl-3-ketotetrahydrofluorene

Bromination in a manner identical with that employed for 2-carbethoxy-3-ketotetrahydrofluorene gave a product m.p. 148°C.

$C_{22}H_{19}O_3Br$ requires 19.5%Br.

Found 20.0%Br.

Reduction of 1-phenyl-3-ketotetrahydrofluorene

The hydrogenation of 1-phenyl-3-ketotetrahydrofluorene in the presence of Raney Nickel in ethanol at 40 lbs./sq.ins. gave only an oil which was ketonic in reaction. The severity of the conditions were increased but no improvement resulted.

7-Benzylidene-8-acenaphthenone (cf. Graebe and Jequier, Ann., 1896, 290, 204).

Equimolar proportions of acenaphthenone and benzaldehyde in ethanol solution were treated with alcoholic caustic soda added dropwise until a violet colour just developed. After standing 6 hours the yellow benzylidene acenaphthenone was removed by filtration and was crystallised as yellow plates (m.p. 117°C) from acetic acid.

7-Phenyl-8-carbethoxy-9-keto-7:8:9:7a-tetrahydrofluoranthene

This was prepared in a manner analogous to the fluorene compound and was obtained in 85% yield, m.p. 188°C. The analysis obtained was not satisfactory but repetition of this work is desirable.

$C_{25}H_{20}O_3$ requires 81.4%C and 5·5%H.

Found 79.5%C and 5·7%H.

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